

## Supplementary Online Content

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**This supplementary material has been provided by the authors to give readers additional information about their work.**

**eTable 1. Search queries used in the different electronic bibliographic databases**

Database	Search query
MEDLINE/ PubMed	(hypersensitivit*[Text Word] OR hypersensitivity[Text Word] OR allerg*[Text Word] OR allergy[Text Word] OR cross-reactiv*[Text Word])  AND (penicillin*[Text Word] OR amoxicillin[Text Word] OR ampicillin[Text Word] OR aminopenicillin[Text Word]) AND  (cefazolin[Text Word] OR cephalosporin*[Title/Abstract])
Web of Science	(TS=hypersensitivit* OR TS=hypersensitivity OR TS=allerg* OR TS=allergy OR TS=cross-reactiv*) AND (TS=penicillin* OR TS=amoxicillin OR TS=ampicillin OR TS=aminopenicillin) AND (TS=cefazolin OR TS=cephazolin OR TS=cephazoline OR TS=ancef OR TS=cephalosporin*)
Embase	(hypersensitiv*:ti,ab,kw OR hypersensitivity:ti,ab,kw OR allerg*:ti,ab,kw OR allergy:ti,ab,kw OR 'cross react*':ti,ab,kw OR 'cross reaction':ti,ab,kw) AND ('penicillin derivative':ti,ab,kw OR penicillin:ti,ab,kw OR amoxicillin:ti,ab,kw OR ampicillin:ti,ab,kw OR aminopenicillin:ti,ab,kw) AND (cefazolin:ti,ab,kw OR cephalosporin*:ti,ab,kw OR cephalosporin:ti,ab,kw OR cephalosporin derivative:ti,ab,kw)

**eTable 2. Characteristics of Included Cohort Studies**

Source, Country	Setting	Age group	Index HS onset	Penicillin HS diagnosis method	Cefazolin HS diagnosis method	N of assessed participants	N of participants with dual allergy (%)
<b>Patients with index penicillin allergy and assessed for cefazolin allergy</b>							
Ahmad et al <sup>17</sup> 2020, USA	Surgical	Not specified	Not specified	Self-reported	Exposure	5	0 (0)
Aihara et al <sup>18</sup> 1987, Japan	Outpatient	Adults, children	Delayed	Skin test, provocation test	Skin test	11	3 (27.3)
Anstey et al <sup>19</sup> , 2019, USA	Surgical	Adults	Immediate, delayed	Self-reported	Exposure	2570	2 (0.1)
Beam et al <sup>20</sup> 1984, USA	Surgical	Adults	Immediate	Skin test	Skin test	2	1 (50.0)
Beltran et al <sup>21</sup> 2015, USA	Inpatient	Adults, children	Immediate, delayed	Self-reported	Exposure	127	1 (0.8)
Blumenthal et al <sup>22</sup> 2019, USA	Inpatient	Adults, children	Immediate, delayed	Self-reported	Provocation test	106	3 (2.8)
Blumenthal et al <sup>23</sup> 2015, USA	Inpatient	Adults	Immediate, delayed	Self-reported	Provocation test	21	1 (4.8)
Castleton et al <sup>24</sup> 1976, UK	Inpatient	Adults	Not specified	Self-reported	Exposure	5	0 (0)
Cook et al <sup>25</sup> 2014, USA	Surgical	Adults	Immediate, delayed	Skin test	Skin test	22	11 (50.0)
Desai et al <sup>26</sup> 2017, USA	Pregnant	Adults	Immediate, delayed	Self-reported	Exposure	1332	10 (0.8)
Desravines et al <sup>27</sup> 2019, USA	Pregnant	Adults	Not specified	Self-reported	Exposure	65	0 (0)
Fonacier et al <sup>28</sup> 2005, USA	Surgical	Adults, children	Immediate, delayed	Self-reported	Exposure	37	0 (0)
Goodman et al <sup>29</sup> 2001, USA	Surgical	Adults	Not specified	Self-reported	Exposure	299	1 (0.3)
Haslam et al <sup>30</sup> et al. 2012, Canada	Surgical	Adults	Delayed	Self-reported	Exposure	54	0 (0)
Laaouaj et al. <sup>31</sup> 2016, USA	Surgical	Adults	Immediate, delayed	Self-reported	Provocation test	139	6 (4.3)

Lam et al. <sup>46</sup> 2020, USA	Surgical	Adults	Not specified	Self-reported	Exposure	500 <sup>a</sup>	0 (0)
Maguire et al. <sup>32</sup> 2020, USA	Emergency department	Adults	Not specified	Self-reported	Provocation test	14	0 (0)
Michaud et al. <sup>33</sup> 2017, Canada	Surgical	Adults	Delayed	Self-reported	Exposure	81	0 (0)
Novalbos et al. <sup>68</sup> 2001, Spain	Outpatient	Adults	Immediate, delayed	Skin test, provocation test	Skin test, provocation test	41	0 (0)
Park et al. <sup>35</sup> 2006, USA	Surgical	Adults, children	Immediate, delayed	Self-reported	Exposure	19	1 (5.3)
Park et al. <sup>36</sup> 2010, USA	Outpatient	Adults	Not specified	Skin test	Exposure	59	1 (1.7)
Pines et al. <sup>37</sup> 1977, UK	Inpatient	Adults	Not specified	Self-reported	Provocation test, exposure	10	1 (10.0)
Ponvert et al. <sup>38</sup> 2011, France	Outpatient	Children	Not specified	Skin test	Skin test	150	0 (0)
Rodriguez et al. <sup>39</sup> 2019, Spain	Outpatient	Adults	Immediate, delayed	Skin test, <i>in vitro</i> , provocation test	Skin test	86	0 (0)
Romano et al. <sup>40</sup> 2020, Italy	Outpatient	Adults	Immediate	Skin test, provocation test	Skin test, provocation test	131	1 (0.8)
Schlosser et al. <sup>41</sup> 2020, USA	Surgical	Adults	Immediate, delayed	Self-reported	Exposure	38	0 (0)
Stone et al. <sup>42</sup> 2019, USA	Surgical	Adults	Immediate, delayed	Self-reported	Exposure	28	0 (0)
Thellier et al. <sup>43</sup> 2020, France	Obstetrics	Adults	Immediate, delayed	Self-reported	Exposure	8	0 (0)
Trubiano et al. <sup>44</sup> 2019, Australia	Outpatient	Adults	Delayed	Skin test, <i>in vitro</i>	Skin test	12	0 (0)
Turner et al. <sup>45</sup> 2018, USA	Inpatient	Adults	Immediate, delayed	Self-reported	Exposure	29	1 (3.4)
<b>Patients with index cefazolin allergy and assessed for penicillin allergy</b>							
Alves et al. <sup>47</sup> 2015, Portugal	Surgical	Adults, children	Immediate, delayed	Provocation test	Skin test, exposure	2	0 (0)
Chng et al. <sup>48</sup> 2016, Singapore	Outpatient s	Adults, children	Immediate, delayed	Skin test	Skin test, provocation test	4	2 (50.0)

Cook et al <sup>25</sup> 2014, USA	Surgical	Adults	Immediate, delayed	Skin test	Skin test	24	11 (45.8)
Farinha et al <sup>49</sup> 2018, Portugal	Surgical	Adults, children	Immediate	Skin test, provocation test	Skin test, exposure test	3	1 (33.3)
Jimenez- Rodriguez et al <sup>39</sup> 2019, Spain	Outpatient, inpatient	Adults	Immediate	Skin test, <i>in vitro</i>	Skin test	3	0 (0)
Kuhlen et al <sup>50</sup> 2016, USA	Surgical	Adults	Immediate	Skin test, provocation test	Skin test, exposure test	5	0 (0)
Laguna et al <sup>51</sup> 2018, Spain	Outpatient	Adults	Immediate	Skin test, <i>in vitro</i> , provocation test	Skin test, provocation test	11	0 (0)
Li et al <sup>52</sup> 2019, Australia	Surgical	Adults, children	Immediate	Provocation test	Skin test, exposure	40	1 (2.5)
Mota et al <sup>69</sup> 2018, Portugal	Surgical	Adults	Immediate	Skin test, <i>in vitro</i> , provocation test	Skin test, exposure	7	0 (0)
Pipet et al <sup>54</sup> 2011, France	Outpatient	Adults, children	Immediate	Skin test, provocation test	Skin test	10	1 (10.0)
Romano et al <sup>56</sup> 2015, Italy	Outpatient	Adults, children	Immediate	Skin test, <i>in vitro</i>	Skin test	6	0 (0)
Romano et al <sup>55</sup> 2010, Italy	Outpatient	Adults, children	Immediate	Skin test	Skin test	2	0 (0)
Uyttebroek et al <sup>70</sup> 2016, Belgium	Surgical	Not specified	Immediate	Skin test, <i>in vitro</i> , provocation test	Skin test, exposure	19	0 (0)
Warrington et al <sup>58</sup> 1996, Canada	Surgical	Adults	Immediate	Skin test	Skin test, exposure	4	0 (0)
Yuson et al <sup>59</sup> 2019, Australia	Outpatient	Adults	Immediate	Skin test, <i>in vitro</i> , provocation test	Skin test, provocation test	6	0 (0)

Abbreviations: HS, hypersensitivity; USA, United States of America; UK, United Kingdom

<sup>a</sup> Estimate sample size based on figure

**eTable 3. Characteristics of case reports Included**

Case study	Sex	Age	Index HS onset	Penicillin HS diagnosis method	Cefazolin HS diagnosis method	Dual allergy to penicillin and cefazolin
<b>Patients with index penicillin allergy and assessed for cefazolin allergy</b>						
Ahmed et al <sup>71</sup> 2012,	Not specified	1	Delayed	Skin test	Exposure	No
Alves et al <sup>47</sup> 2015	F	50	Immediate	Skin test	Exposure	No
Berrocal et al <sup>72</sup> 2001	F	70	Immediate	Self-reported	Exposure	Yes
Castro et al <sup>73</sup> 1996	M	3	Delayed	Skin test, provocation test	Skin test	No
Christen et al <sup>74</sup> 1990	M	43	Delayed	Self-reported	Exposure	No
Eser Simsek et al <sup>75</sup> 2018	F	10	Immediate	Skin test, provocation test	Provocation test	No
Fitzgerald et al <sup>76</sup> 2016	Not specified	66	Immediate	Self-reported	Exposure	No
Freedman et al <sup>77</sup> 1997	F	40	Not specified	Self-reported	Exposure	No
Gonzalez-Delgado et al <sup>78</sup> 2006	F	7	Delayed	Skin test, patch test	Skin test, patch test	No
Ho et al <sup>79</sup> 2004	F	74	Delayed	<i>in vitro</i>	<i>in vitro</i> IgE	No
Jao et al <sup>80</sup> 2006	F	37	Not specified	Self-reported	Exposure	Yes
Kraushar et al <sup>81</sup> 1994	F	72	Not specified	Self-reported	Exposure	Yes
Moake et al <sup>82</sup> 1978	F	39	Immediate	<i>in vitro</i>	<i>in vitro</i> IgE	Yes
Nemati et al <sup>83</sup> 1981	M	24	Delayed	Self-reported	Exposure	Yes
Philips et al <sup>84</sup> 2001	Not specified	Not specified	Delayed	Skin test, patch test	Skin test	Yes
Vogt et al <sup>85</sup> 1998	F	46	Delayed	Self-reported	Exposure	No
<b>Patients with index cefazolin allergy and assessed for penicillin allergy</b>						
Almeida et al <sup>86</sup> 2017	F	36	Immediate	Provocation test	Skin test, <i>in vitro</i> IgE	No
Almeida et al <sup>86</sup> 2017	F	49	Immediate	Provocation test	Skin test, <i>in vitro</i> IgE	No
Chan et al <sup>87</sup> 2016	Not specified	Not specified	Immediate	Skin test	Skin test	Yes
Culp et al <sup>88</sup> 2017	M	44	Immediate	Skin test, <i>in vitro</i>	Exposure	No

Gonzalo-Garijo et al <sup>89</sup> 2006	F	66	Not specified	Skin test, provocation test	Skin test	No
Igea et al <sup>90</sup> 1992	F	21	Immediate	Skin test, provocation test	Skin test, <i>in vitro</i> IgE	No
Igea et al <sup>90</sup> 1992	F	45	Immediate	Skin test, provocation test	Skin test, <i>in vitro</i> IgE	No
Lee et al <sup>91</sup> 2004	F	46	Immediate	Skin test	Skin test	No
Padial et al <sup>92</sup> 2008	Not specified	43	Delayed	Skin test, provocation test	Skin test, provocation test	No
Pinheiro et al <sup>93</sup> 2018	F	31	Delayed	Patch test	Patch test	Yes
Romano et al 2001 <sup>94</sup>	F	44	Delayed	Skin test, patch test, <i>in vitro</i> , provocation test	Skin test, patch test, <i>in vitro</i> IgE, provocation test	No
Romeira et al <sup>63</sup> 2017	Not specified	Not specified	Not specified	Skin test	Skin test	No
Somech et al <sup>95</sup> 2009	M	12	Immediate	Skin test, provocation test	Skin test	No
Tayman et al <sup>96</sup> 2008	F	0	Immediate	Skin test, <i>in vitro</i>	Skin test, <i>in vitro</i> IgE	Yes
Velasco et al <sup>97</sup> 2009	F	63	Delayed	Skin test, patch test, <i>in vitro</i> , provocation test	Skin test, patch test, <i>in vitro</i> IgE, provocation test	No
Vieira et al <sup>98</sup> 2009	M	32	Immediate	Skin test, <i>in vitro</i>	Skin test	No
Weber et al <sup>99</sup> 1996	F	33	Immediate	Skin test, provocation test	Skin test	No
Wieczorek et al <sup>100</sup> 2008	F	18	Immediate	Skin test, <i>in vitro</i> , provocation test	Skin test, <i>in vitro</i> IgE	No
Yun et al <sup>101</sup> 2016	M	26	Immediate	Skin test	Skin test	No
<b>Patients with index beta-lactam allergy and assessed for penicillin and cefazolin allergy</b>						
Classen et al <sup>102</sup> 2015	F	24	Not specified	Skin test	Skin test, patch test	Yes
Gonzalo-Garijo et al <sup>89</sup> 2006	M	80	Not specified	Skin test, provocation test	Skin test	No
Rozlucka et al <sup>103</sup> 2019	Not specified	65	Not specified	Skin test, provocation test	Skin test, provocation test	No

**eTable 4. Risk of bias of individual studies**

Study	Risk of Bias				
	Representation of the target population	Consecutive sampling	Non-response bias	Definition of the allergic reaction	Consistency of data collection / assessment
<b>Studies assessing patients with index penicillin allergy (tested for cefazolin)</b>					
Castleton B (1976)	●	●	●	●	●
Pines A (1977)	●	●	●	●	●
Beam TR (1984)	●	●	●	●	●
Aihara M (1987)	●	●	●	●	●
Goodman EJ (2001)	●	●	●	●	●
Novalbos A (2001)	●	●	●	●	●
Fonacier L (2005)	●	●	●	●	●
Park M (2006)	●	●	●	●	●
Park M (2010)	●	●	●	●	●
Ponvert C (2011)	●	●	●	●	●
Haslam S (2012)	●	●	●	●	●
Cook DJ (2014)	●	●	●	●	●
Beltran RJ (2015)	●	●	●	●	●
Blumenthal KG (2015)	●	●	●	●	●
Laaouaj J (2016)	●	●	●	●	●

Desai SH (2017)	●	●	●	●	●
Michaud L (2017)	●	●	●	●	●
Turner NA (2018)	●	●	●	●	●
Astey K (2019)	●	●	●	●	●
Blumenthal KG (2019)	●	●	●	●	●
Desravines N (2019)	●	●	●	●	●
Jimenez-Rodriguez T (2019)	●	●	●	●	●
Schlosser KA (2019)	●	●	●	●	●
Thellier C (2019)	●	●	●	●	●
Trubiano J (2019)	●	●	●	●	●
Ahmad H (2020)	●	●	●	●	●
Lam PW (2020)	●	●	●	●	●
Maguire M (2020)	●	●	●	●	●
Romano A (2020)	●	●	●	●	●
<b>Studies assessing patients with index cefazolin allergy (tested for penicillins)</b>					
Warrington RJ (1996)	●	●	●	●	●
Romano A (2010)	●	●	●	●	●
Pipet A (2011)	●	●	●	●	●
Cook DJ (2014)	●	●	●	●	●
Alves C (2015)	●	●	●	●	●
Romano A (2015)	●	●	●	●	●
Chng H (2016)	●	●	●	●	●
Kuhlen JL (2016)	●	●	●	●	●
Uyttebroek AP (2016)	●	●	●	●	●
Farinha SM (2018)	●	●	●	●	●
Laguna JJ (2018)	●	●	●	●	●
Mota I (2018)	●	●	●	●	●
Jimenez-Rodriguez T (2019)	●	●	●	●	●
Li J (2019)	●	●	●	●	●
Yuson C (2019)	●	●	●	●	●

**Legend:** ● - Low risk of bias; ● - Unclear risk of bias; ● - High risk of bias.