

# Journal Pre-proof

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PII: S2213-2198(20)30032-5

DOI: <https://doi.org/10.1016/j.jaip.2019.12.034>

Reference: JAIP 2622

To appear in: *The Journal of Allergy and Clinical Immunology: In Practice*

Received Date: 8 September 2019

Revised Date: 23 December 2019

Accepted Date: 26 December 2019

Please cite this article as: HI A, Vazquez-Ortiz M, AW M, EM M, De-Labeling Penicillin-Allergic Children In Outpatients Using Telemedicine: Potential To Replicate In Primary Care, *The Journal of Allergy and Clinical Immunology: In Practice* (2020), doi: <https://doi.org/10.1016/j.jaip.2019.12.034>.

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# **DE-LABELLING PENICILLIN-ALLERGIC CHILDREN IN OUTPATIENTS USING TELEMEDICINE: POTENTIAL TO REPLICATE IN PRIMARY CARE**

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**Financial disclosure:** The authors have no financial relationships relevant to this article to disclose.

**Funding source:** This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

**Potential Conflicts of Interest:** The authors have no conflicts of interest relevant to this article to disclose.

**Word Count:** 996

**Clinical Implications:** Penicillin-allergy label from childhood is common and mainly spurious. A pragmatic, primary care physician (PCP)-led approach to de-labelling penicillin allergy in children using telemedicine screening followed by single dose oral challenge is feasible, safe and acceptable to parents.

**To the Editor:**

Up to 5% of children are inappropriately labelled 'penicillin-allergic', commonly in the context of a viral rash, leading to use of alternative antibiotics and poorer health outcomes [1].

Investigating these mostly 'low probability' patients poses a significant burden on allergy services.

There is no unified consensus on penicillin-allergy de-labelling in children. Blood/skin testing are limited in sensitivity and specificity [2] and restricted to specialist services [2, 3].

Currently, direct drug provocation testing (DPT), without previous skin/blood testing, is acceptable in children labelled 'penicillin-allergic' due to prior mild cutaneous reactions [1, 2, 4-6].

In many countries, there is a general shift to move less specialised tasks to primary care. An expert review suggested telemedicine might be useful to triage adult allergy clinics [7].

This study was performed by a Primary Care Physician (PCP) as part of an MSc in Allergy. All components of the study were performed solely by the PCP including telemedicine for screening/risk stratification, performance of single dose oral challenge in a secondary care outpatient department resembling resources available in primary care, supervision of all patients for 2 hours post-challenge and follow-up teleconsultation. No additional personnel were required. A Paediatric allergist was available to discuss the few unclear cases. The aim was to de-label 'penicillin-allergic' children at low probability of true allergy, without preceding skin/blood testing, exploring potential for future replication in primary care. The study aimed to include all beta-lactams. However, only aminopenicillin-allergic labelled children were finally recruited; thus, this manuscript focuses on penicillin-allergy only.

Children aged 1 to 17 years old were invited and screened via structured teleconsultation (**Table E1**). Candidates considered at very low likelihood of penicillin-allergy on tele-screening were deemed 'low probability' (**Table 1**) and attended an outpatient visit. In cases where the parent was unable to recall the history accurately, 'low probability' was based on the absence of cardiorespiratory/severe symptoms at the index event and excluded poorly controlled asthma [8]. A study-specific appointment in outpatients was scheduled. Written consent obtained. Children were verbally confirmed clinically well. Temperature, weight and cardiorespiratory examination performed. A single, age-appropriate dose of penicillin administered. If the index penicillin was unknown, amoxicillin, the local recommended first-line antibiotic, was used. Visual/verbal assessment was performed every 30 minutes for 2 hours; following this, the child was verbally confirmed clinically well and skin examination performed. (**Table E2**) A 5-day penicillin course prescribed to negative challenge participants. Follow-up teleconsultation (**Table E3**) on Day 6 post-challenge assessed for hypersensitivity reaction, parental satisfaction, willingness to use penicillin in the future and attitude to undergoing a challenge in primary care or at home.

140 children were invited to partake, 90 from primary care, 32 from secondary care, 18 self-referrals; 136 underwent telemedicine screening (**Figure 1**). Mean age was 8.2 years (SD: 4.4 years). Sixteen children were considered 'high probability' requiring referral to specialist allergy service; the remaining 118 (87%) were considered 'low probability' including 58 whose parents could not recall accurate history details, but had no features suggesting cardiovascular or severe symptoms or poorly controlled asthma. Two children ('other') received the suspected penicillin safely after the index reaction and were automatically de-labelled.

Of 118 'low probability' children, 16 (14%) withdrew prior to DPT and 102 (86%) completed the DPT. No child had an immediate reaction at DPT; 96/102 (94%) had no symptoms following the 5-day home course. Three (2.9%) children developed a non-immediate

morbilliform rash at home and were considered 'allergic'. Three (2.9%) children reported mild/subjective gastrointestinal symptoms during the 5-day home course and were considered unlikely allergic by two drug allergy experts consulted. This pragmatic approach allowed 99/102 (97%) 'low probability' children to be de-labelled.

Overall 120/140 (86%) families invited to partake engaged with de-labelling including completion of a 5-day penicillin course for 98/102 (96%). Parents reported high levels of satisfaction, assessed on a scale of 0-10 (0=extremely unhappy, 10=extremely happy); 89/102 (87%) scored 10/10; 6 scored 9/10; 5 scored 8/10; 1 scored 6/10 and 1 did not score. In total, 98/102 (96%) reported confidence using penicillin in the future; 87/102 (85%) reported confidence to undergo a similar de-labelling process in primary care (63 expressed preference for DPT to be carried out in primary care, 24 either primary care or at home), whilst 15 parents preferred DPT done in hospital.

This study found less than 3% of 'low probability', labelled children were confirmed penicillin-allergic. To the best of our knowledge, this is the first PCP-led study of drug allergy using telemedicine as a screening/risk stratification tool for de-labelling penicillin-allergy in children and assessing parental attitudes to undergoing a similar process in primary care.

The single dose DPT in 'low probability' patients, without preceding allergy testing, was shown to be safe with no immediate reactions. The protocol was acceptable to patients and families as 86% (102/118) of patients eligible for single dose DPT completed the process and 96% (98/102) completed the home course of antibiotics. Limitations include the small sample size and 5-day home course antibiotics, which more recent evidence suggests is prolonged [9].

Our study results reinforce the need to de-label penicillin-allergy in children. The reality of primary care is that most paediatric 'penicillin-allergy' labelling is false. It opens new clinical

and research opportunities for potentially more feasible and cost-effective approaches to penicillin de-labelling, including upskilling of PCPs and use of telemedicine for screening/risk stratification. Although DPTs are not currently performed in primary care, these data suggest this might be an acceptable option, for example by setting up reference dedicated penicillin-allergy clinics covering a particular area, run by an allergy-trained PCP, linked to a regional allergy service for particular queries.

Spurious penicillin-allergy labelling is a major public healthcare concern. This study presents a practical, effective, safe and highly rated approach to de-labelling children with low probability of penicillin-allergy. This includes telemedicine as a screening and follow-up tool, and a simplified single dose DPT, led by an allergy-trained PCP. This opens new clinical and research opportunities for community-based approaches to de-labelling 'low probability' penicillin-allergy, taking the burden off more specialised hospital-based allergy services.

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188 **Table 1: Screening criteria for risk stratification and decision on further work-up.**

| <b><u>'High probability'</u>, (requiring referral to specialist allergy service)</b>                                                                                                                        | <b><u>'Low probability'</u>, (eligible for pragmatic de-labelling approach)</b>                                                                                                                                                                                                                                                                         |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Immediate symptoms suggestive of an IgE-mediated allergic reaction (e.g. urticaria, angioedema) less than 1 hour of having the drug<br>OR airway, breathing or central nervous system involvement <u>OR</u> | Child 1 to 17 years old <u>AND</u>                                                                                                                                                                                                                                                                                                                      |
| Urticarial rash or angioedema occurring >1 hour of having the drug and resolving within 12 hours <u>OR</u>                                                                                                  | Absence of all 'high risk' criteria <u>AND</u>                                                                                                                                                                                                                                                                                                          |
| >1 reaction with the same or different Beta-lactam antibiotic <u>OR</u>                                                                                                                                     | Non-immediate (>1 hours) episode of skin rash or other symptoms compatible with an allergic reaction after penicillin antibiotic administration in childhood. This may include urticarial rash or angioedema occurring > 1 hour after having the drug and persisting >12 hours of having the drug, non-responsive to antihistamine medication <u>OR</u> |
| "Atypical" potentially severe drug reactions such as SJS, DRESS syndrome or TEN <u>OR</u>                                                                                                                   | Family history of penicillin allergy resulting in penicillin avoidance <u>OR</u>                                                                                                                                                                                                                                                                        |
| Suspected reactions to parenteral penicillin antibiotics <u>OR</u>                                                                                                                                          | Non-allergic reaction to penicillin, such as gastrointestinal disturbance, or other symptoms not consistent with an allergic reaction                                                                                                                                                                                                                   |
| Insufficiently controlled asthma [8]                                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                         |

189 SJS, Stevens-Johnson syndrome; DRESS, Drug reaction with eosinophilia and systemic  
 190 symptoms; TEN, Toxic Epidermal Necrolysis.

**Figure 1: Summary of Results**

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## Results Flow Chart

