# Anti-insulin antibody concentration in type 1 diabetes mellitus patients injecting different types of insulin

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## Background

Regulatory guidelines for insulin products development require to test immunogenicity in a reasonable number of patients with type 1 diabetes mellitus (T1DM).

The problem of sample size for immunogenicity comparison is substantial in insulin biosimilar development since the required samples are sizeable however still incapable to detect any immunogenicity difference, because the biosimilar and a reference drug are very similar in all terms.

The data on immunogenicity of different insulin products is controversial. Some works show no difference in immunogenicity between different insulin INN, but some show more immunogenic INNs. The controversy might be due to immunogenicity testing methods and sensitivity of the tests.

However, the absolute difference regardless its statistical significance seems to be clinically miniscule.

## Aim

To estimate the input of insulin product into immune response development.

## Methods

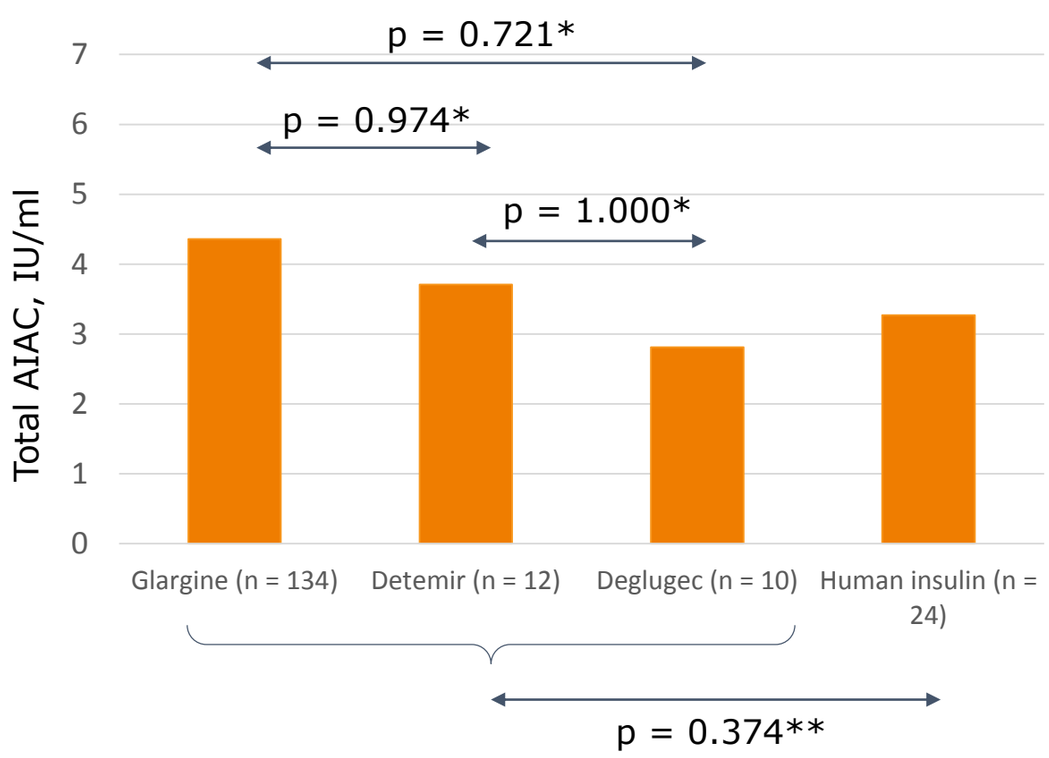
Blood samples of 180 adult patients with T1DM for at least 12 months before screening treated with stable daily insulin doses in basal-bolus regimen for at least 30 days before screening, with HbA1c level 6.5–12.0% were taken to estimate an anti-insulin antibody concentration (AIAC) via enzyme-linked immunosorbent assay.

The information on insulin international non-proprietary name (INN) was gathered.

Influence of basal and bolus insulin INNs on AIAC was estimated with ANOVA. One-to-one comparisons were made with Mann-Whitney U-test.

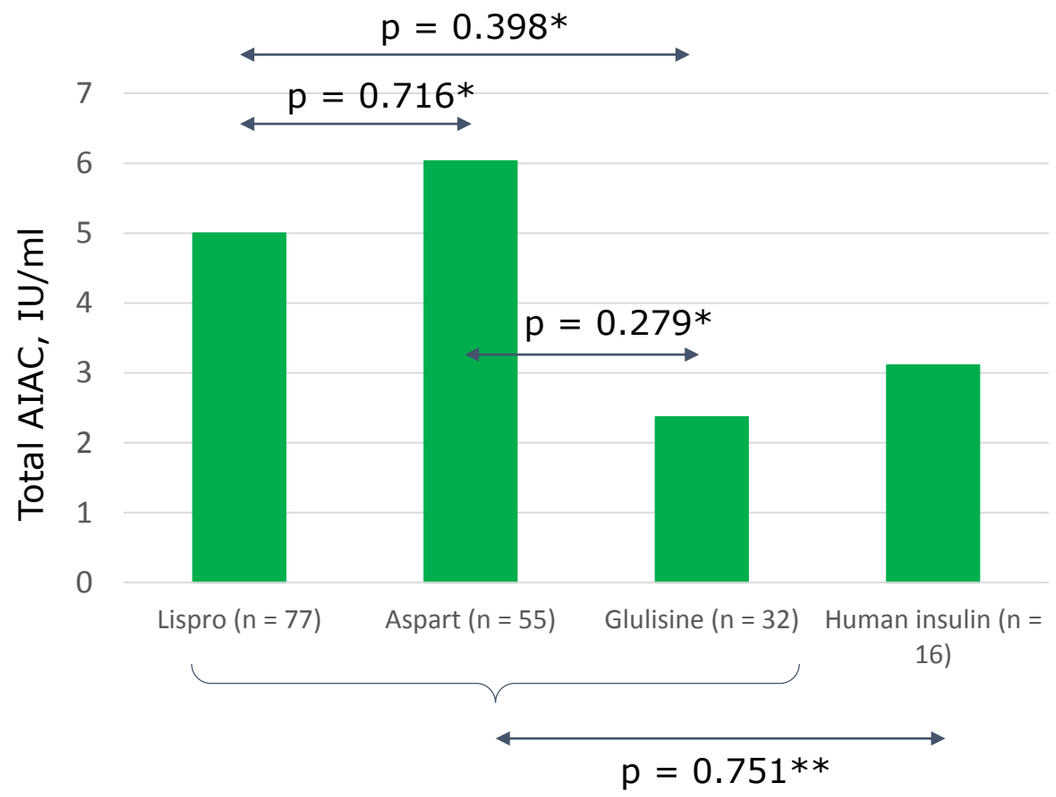
## Results

Basal insulins (p=0.765)




*Mann-Whitney U-test, Bonferroni correction
**Mann-Whitney U-test

Bolus insulins (p=0.283)

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## Conclusions

The input of insulin product into immune response development was nonsignificant, thus the huge sample is required to detect immunogenicity difference.

This leads to dramatic increase of clinical trials cost and breaks the idea of cost-affordable biosimilars. Thus immunogenicity risk assessment should be provided mostly at preclinical stage, and immunogenicity should be studied via pharmacovigilance.

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