

# Changes in the Microbiome of Children with Type 1 Diabetic

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## Introduction

Type 1 Diabetes (T1D) is an autoimmune disease where  $\beta$ -cells of the pancreatic islets are destroyed, reducing the insulin secreted and preventing simple carbohydrate absorption (1). Currently, approximately 70% of T1D diagnosis carry the susceptibility mutation on the HLA alleles, however only 3-7% of these carriers develop T1D (2). Therefore, the majority of recorded T1D cases are not due to genetic predisposition, implying that the prevalence is associated with environmental, nongenetic factors. A proposed link between T1D and nongenetic factors is the role of the gut microbiome. Initially established in utero and early childhood, the gut microbiome can play an important role in one's metabolism, nutrient absorption, physiology and immune function (3, 4). This link has been investigated by multitude of studies with this review outlining some of the crucial findings of these papers.

## Aims

To investigate whether the current literature is providing evidence that there is a link between onset of T1D and the microbiome.

## Methods and Materials

Search for primary literature was done using PubMed Central.

## Results

Studies have identified two main causes of temporal instability on the gut microbiome of children aged between 2 and 3 – cessation of breastfeeding and age.

## Age as a factor

Adding further to age as a factor for nongenetic predisposition for T1D, incorporation of solid foods during development can have an impact on the microbiome. Diversification of diet accounts to increased  $\alpha$ -diversity (mean species diversity) of the gut microbiome, due to naturally present microorganisms in and on food, as well as to accommodate metabolism of varied nutrients (2, 1). Additionally, the number of distinct microorganisms in a community increases exponentially until the age of 3, with 10% of bacterial strains maintained from infancy until the age of 3, while  $\beta$ -diversity (difference between the microbial composition of 2 or more environments) is found not to be age dependent (2). Interestingly, individuals with confirmed T1D observed a decrease in  $\alpha$ -diversity, while non-converted and seroconverted individuals'  $\alpha$ -diversity was exponentially increasing (Figure 1).

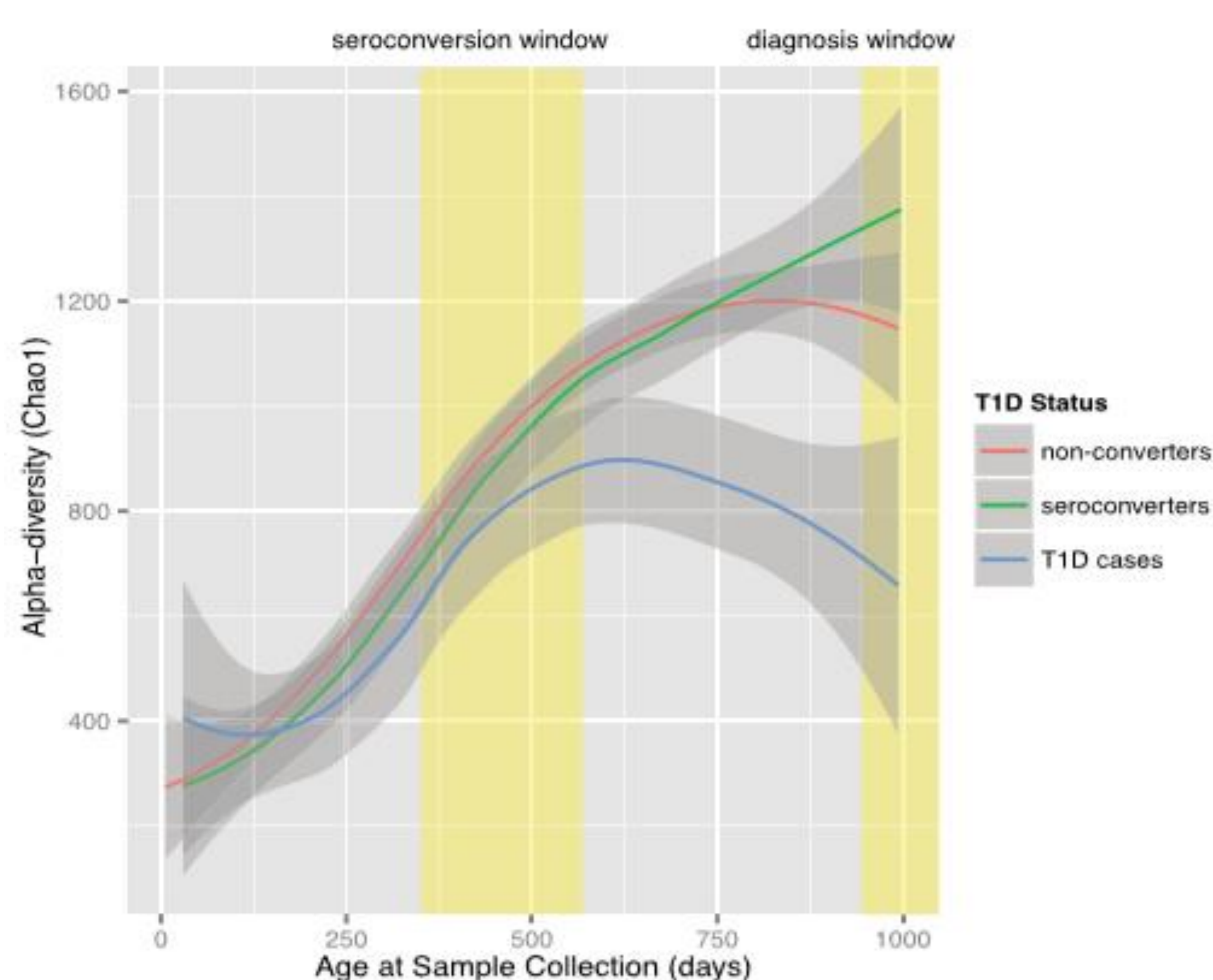


Figure 1. Chao1 alpha-diversity plot of  $\alpha$ -diversity of non-converted, seroconverted and T1D diagnosed individuals (2)

## Cessation of breast feeding as a factor

During early development, an increase of *Bifidobacterium* species, facilitating lactose degradation using lactase dehydrogenase has been observed from month 1 until approximately month 14 (1). However, in the research of Endesfelder *et al* (2016) at the 6 month point, an increase of the phylum Proteobacteria, comprised mostly of *Enterobacteriales* and *Lactobacillales* species has been observed. Additionally, past the 6 months mark, with introduction of solid foods, a reduction of the aforementioned phylum and an increase of Firmicutes, Ruminococcus and Blautia was noted (3), which are phyla characteristic of an adult-like microbiome. Comparatively, in cases of children diagnosed with T1D, an increase of *Streptococcus*, *Ruminococcus* and *Lactococcus* species has been observed (2, 1), which are considered pathobionts, inducing inflammation in the gut. Additionally, these species have been found to be overabundant in T1D cases and seroconverters had an intermediate abundance, when compared to nonconverted individuals, identifying that there is a shift in microbial communities even before T1D diagnosis (Figure 2).

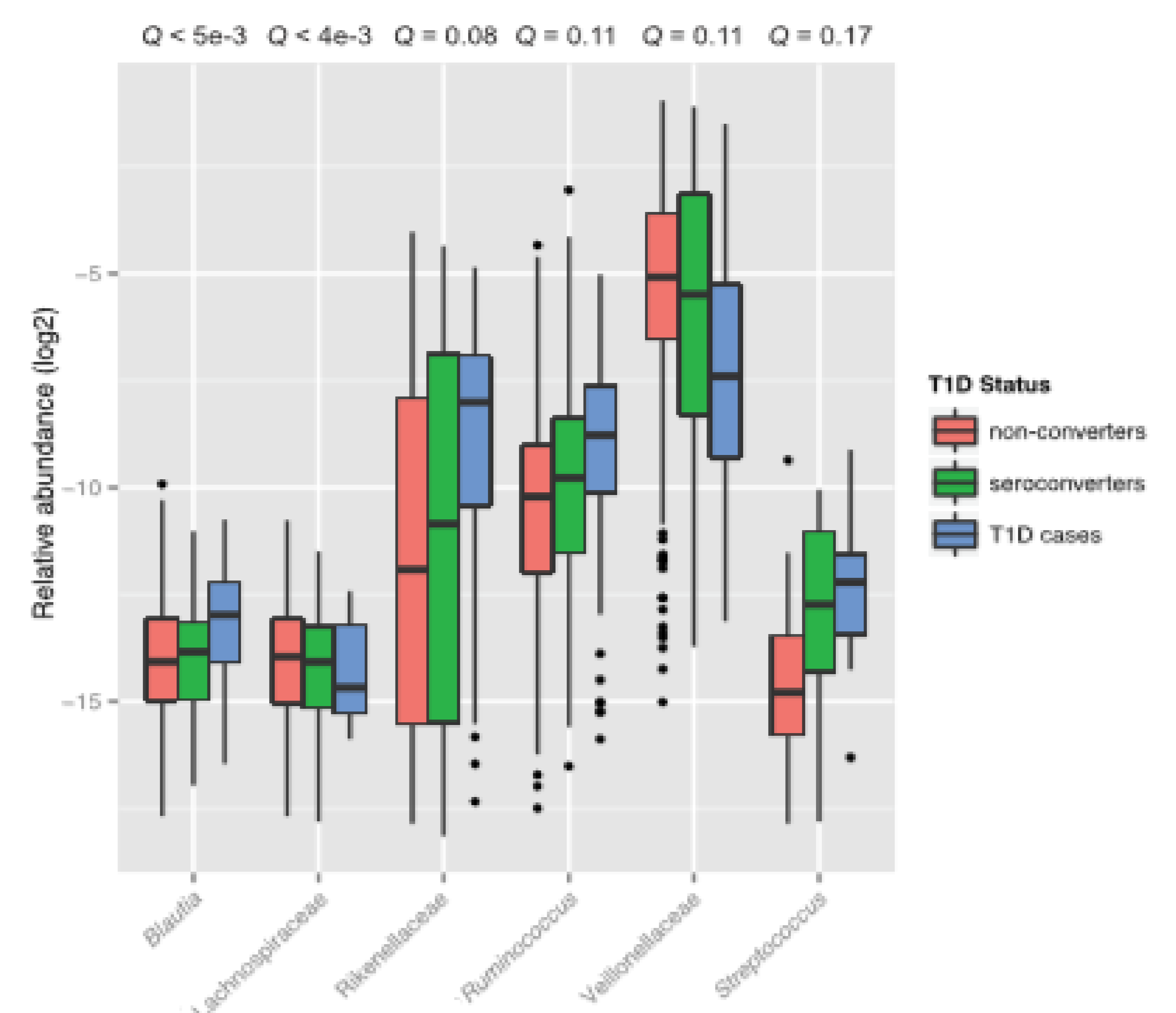


Figure 2. Differences in microbial abundance of non-converted, seroconverted and T1D diagnosed individuals, where overabundance of Blautia, Ruminococcus and Streptococcus is observed (2)

## Discussion

- It is currently unknown what are the causations of overgrowth of Blautia, Ruminococcus and Streptococcus within the gut and despite some evidence we can currently speculate at what age these species are being introduced, regardless of food intake.
- The overabundance of Blautia, Ruminococcus and Streptococcus in T1D children cannot only cause gut inflammation but also induce permeability of the gut epithelium.
- The positive correlation between Bacteroides and anti-islet antibodies advances the further destruction of  $\beta$ -cells and aiding disease onset.
- Potential stabilisation of the microbiome using faecal microbial transplant from non-converted to seroconverted / T1D individuals, could likely have a suppressive effect on production anti-islet antibodies and gut inflammation by establishing the non-converted individuals' microbiome.
- Future research could concentrate on broadening the knowledge of microbial communities, including fungal, archaeal and viral diversity.

## Bibliography

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