1. **What is the main question the paper answers? Identify the question and any hypotheses the authors mention. Is this related to a set of observations, a long-standing question, or a theoretical prediction?**

   The main question the paper attempts to answer is whether or not microbe diversity and microbe exposure has an impact on the prevalence of Alzheimer’s disease. The authors hypothesize that where there is lower microbe diversity and exposure, there will be more cases of Alzheimer’s. This hypothesis was based on previous observations that autoimmune disorders are less common in areas with a high diversity of microbes. The causes of Alzheimer’s are thought to be similar to those of autoimmunity, so the researchers thought the diversity of microbe exposure may also affect Alzheimer’s rates.

2. **Was the study well designed to address the hypothesis (or hypotheses)?**

   Yes, the study was well designed to address the hypothesis—the study focuses on microbe diversity, microbe exposure, and Alzheimer’s rates in various places throughout the world. The researchers also controlled for varying lifespans and causes of death prior to the age of the typical onset of Alzheimer’s.

3. **What are the data presented in the paper? If they presented actual data, what was their sample size (e.g., people, animals, or habitats, etc.)?**

   The data presented in this paper includes data from WHO’s Global Burden of Disease report published in 2009, specifically the cases of Alzheimer’s disease adjusted for the varying lifespans throughout the world. Additionally, the authors also presented data on pathogen prevalence across 192 countries taken from a variety of sources.

4. **What did the researchers conclude and do they provide enough evidence to support their conclusion?**

   The researchers concluded that the countries with lower microbe diversity and lower microbe exposure have a higher number of Alzheimer’s cases. They provided enough evidence to support their conclusion since this conclusion was based on several countries evaluated throughout the world. The conclusions are based on correlations, so they cannot say whether high microbial diversity actually reduces chances of Alzheimer’s, but they provide enough evidence to claim there is a correlation.

5. **What possible explanations for the results are considered in the article? Do they cover all the possibilities? Is each explanation given fair consideration?**

   The article really only focused on one possible explanation for the conclusions that they made. The explanation is known as the old friends hypothesis. This hypothesis states that human immune systems have evolved alongside many types of germs that may help the body prepare to defend against lethal microbial invaders. However, in today’s modern society where people are hygiene and sanitization conscious, there is decreased exposure to the “friendly” microbes that have helped immune systems evolve to function properly. This mismatch of the immune system and its usual environment may then lead to immune system dysfunction, which is related to autoimmunity and potentially Alzheimer’s.
6. Did the researchers identify any issues with their data or methods? Were there any issues they didn’t mention?
There were two main issues that the researchers identified in regards to their data/methods. One such issue was that for some countries, health reports are often based off of estimates and projections rather than firm counts. The second issue that the researchers identified was that large-scale epidemiological studies are based on correlational studies and cannot demonstrate causality. While this is true, seeking causality in any health-related study has potential ethical issues.

7. What could the researchers have investigated more thoroughly or explained better?
The researchers could have better explained their methods since at times they were hard to follow. Additionally, a lot of technical terms related to the immune system were used that could have been explained a little bit better. Aside from that, it seems to be a thorough correlative investigation and a well-detailed paper.

8. Why is this study important? Was it interesting to you? (And if so, why?)
This study is important because it opens up the potential to understand different issues that may be responsible for increased rates of Alzheimer’s disease. Alzheimer’s is still such a mystery and is a devastating disease for which we do not yet have a cure; this study seemed to provide some valuable insight on the pathology of this disease.