**Introduction**

Organisms who are born small for gestational age, or who experience early growth faltering have the opportunity for catch-up growth should environmental conditions improve (Boersma and Wit 1997; Singhal 2017; Wells 2018; Metcalfe and Monaghan 2001). Catch-up growth is marked by rapid weight or height gain following a period of restricted development [(Boersma and Wit 1997](https://www.zotero.org/google-docs/?IVMfpf); [Hornick et al. 2000)](https://www.zotero.org/google-docs/?FpUsF6). During a catch-up phase, elevated growth rates allow a young organism to either approach, or reach its genetically-predetermined, “normal” growth curve [(Boersma and Wit 1997)](https://www.zotero.org/google-docs/?MP8AgG). However, there is evidence that such accelerated growth may carry deleterious long-term health effects, suggesting a physiological cost of growth [(Singhal 2017; Metcalfe and Monaghan 2001; Wells 2018)](https://www.zotero.org/google-docs/?n2f9d2).

The idea that growth carries a biological cost is supported by life history theory, which treats energy as a finite resource that must be partitioned to fitness components. Organisms differentially allocate energy between growth, survival, or reproduction [(Jones 2011)](https://www.zotero.org/google-docs/?broken=F9g0mp). The optimal allocation strategy is under selection to maximize fitness. During a period of catch-up growth, it is expected that energy would be diverted away from cell maintenance. Such a process favors immediate survival and early reproduction over future survival, thus decreasing future life expectancy [(Wells 2018; Metcalfe and Monaghan 2001)](https://www.zotero.org/google-docs/?broken=WOl5Q1). Based on this model, we would expect more rapid growth to require an even greater energetic input at the further cost of maintenance functions.

The potential cost of accelerated growth has been investigated in multiple non-human species. Catch-up growth in three-spined sticklebacks (*Gasterosteus aculeatus*) has been shown to substantially decrease median lifespan, and faster growth in King Penguin (*Aptenodytes patagonicus*) chicks is associated with increased oxidative damage and telomere loss [(Lee, Monaghan, and Metcalfe 2013; Geiger et al. 2012)](https://www.zotero.org/google-docs/?F15owD). Evidence suggests that early catch-up growth in humans is indicative of non-communicable disease risk and a shorter lifespan [(Metcalfe and Monaghan 2001; Singhal 2017)](https://www.zotero.org/google-docs/?kHMDBT). However, the relationship between catch-up growth and human mortality is more difficult to study due to the prevalence of confounding factors and ethical concerns, as well as logistical complications associated with the length of the human lifecycle [(Lee, Monaghan, and Metcalfe 2013; Boersma and Wit 1997)](https://www.zotero.org/google-docs/?j9gowb).

Here we investigate the hypothesized human life-history tradeoff between growth, maintenance, and survival using epigenetic clocks: a recent biomarker that accurately predicts cellular aging and age related health outcomes early in the life cycle. Epigenetic clocks allow for insight into epigenetic, chronological, and biological age. Epigenetic age, or DNAm age, is measured by the proportion of methylated CpG sites within the DNA of a given sample [(Ryan 2021; Horvath and Raj 2018)](https://www.zotero.org/google-docs/?kmAcRX). DNA methylation occurs at predictable rates, allowing for an accurate estimate of chronological age, and a proxy for predicting life-cycle changes [(Ryan 2021](https://www.zotero.org/google-docs/?K8s9OP); Bocklandt et al. 2011). Deviations from chronological age, however, do occur. The difference between chronological and epigenetic age is referred to as biological age [(Ryan 2021)](https://www.zotero.org/google-docs/?bsDIPu). Biological age measures senescence, as well as age-related disease and mortality risk [(Field et al. 2018)](https://www.zotero.org/google-docs/?jlCB5A). An individual who appears epigenetically older, and thus biologically older than anticipated, displays positive age acceleration-- a phenomenon which predicts elevated mortality risk among adults [(Horvath and Raj 2018; Ryan 2021; Simpkin et al. 2016; )](https://www.zotero.org/google-docs/?3ZCXjP).

Epigenetic age increases more rapidly during periods of growth, and is associated with certain childhood developmental changes [(Horvath and Raj 2018; Simpkin et al. 2016; 2017)](https://www.zotero.org/google-docs/?spZ986). Childhood and adolescent accelerated epigenetic age can persist into adulthood, where it predicts elevated mortality risk [(Horvath and Raj 2018)](https://www.zotero.org/google-docs/?Ptrb4R). Our study aimed to relate catch-up growth with age acceleration using data from the Cebu Longitudinal Health and Nutrition Survey (CLHNS)--a cohort study started in 1983 that has collected data on relevant nutrition, health, and demographic questions in N subsequent generations [(Adair et al. 2011)](https://www.zotero.org/google-docs/?3qGB3U). Using epigenetic clocks, we examined adult epigenetic age and determined if individuals who experienced childhood catch-up growth appear biologically older than expected. We predict a positive relationship between early growth rate and epigenetic age in adulthood. This association would indicate a biological cost of growth, and a life-history tradeoff between cell maintenance and development.

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