

## Black-Box Optimization for Sample Size Determination in Interrupted Time Series (ITS) Design

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**Introduction :** Interrupted time series (ITS) design is a quasi-experimental design used to estimate the causal effect of an intervention by comparing pre- and post-intervention structural changes in the time series, including level, slope, and potentially seasonality or autocorrelation. Sample size determination (SSD) is essential for appropriate inference, yet analytical formulas for ITS are rarely available due to the complexity of the design and the involvement of multiple parameters. Consequently, existing methods rely on computationally intensive grid search or simulations, hindering practical use.

**Methods :** We propose applying black-box optimization (BBO) to SSD in ITS designs. BBO is well-suited for problems where objective functions are mathematically intractable. We focus on Bayesian Optimization (BO) as a representative BBO algorithm, given its efficiency for problems involving costly evaluations. Building on the framework of Hawley et al. (2018), we formulate SSD as a constrained multi-objective optimization problem: minimizing both the number of time points and number of samples per point, subject to prespecified type I error and statistical power requirements. Both level-change and slope-change ITS models were considered, using a binary outcome as in Hawley et al. (2018).

**Results :** Preliminary experiments demonstrated faster computation and improved precision compared with grid search. For example, settings that previously required several minutes could be identified substantially faster (within about one minute in our preliminary runs) using BO. Further practical procedures for SSD and corresponding visualizations will be presented at the conference.

**Conclusion :** This approach provides a more efficient solution to the practically demanding problem of SSD in ITS designs, and offers a versatile framework applicable to more complex settings where analytical formulas are unavailable.

## Conversational AI Agents and Well-Being: Moderating Effects of Social Ties and Loneliness

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**Introduction :** Conversational AI agents, such as Replika and Character.AI, are increasingly used for emotional support. However, their psychological effects remain underexplored. This study examined whether the use of conversational AI agents is associated with enhanced subjective well-being, and whether these associations are moderated by social connectedness and loneliness.

**Methods :** We analyzed cross-sectional data from 14,721 Japanese adults who completed nationwide internet surveys in December 2024 and January 2025. Subjective well-being was assessed across three domains: life satisfaction, happiness, and sense of purpose. Participants were categorized as users of conversational or non-conversational AI. Social connectedness was measured using the Lubben Social Network Scale (LSNS-6), and loneliness using the UCLA Loneliness Scale. Multivariable linear regression and restricted cubic spline models were applied.

**Results :** Use of conversational AI agents was significantly associated with higher well-being scores across all three domains. In contrast, non-conversational AI use showed weaker or inconsistent associations. A U-shaped moderation pattern was observed: the associations of conversational AI agents were most pronounced among individuals with moderate levels of social connection and diminished among those with either low or high levels. The strongest positive associations were observed among individuals reporting high loneliness.

**Discussion :** Conversational AI agents may offer psychological benefits, particularly for those with unmet emotional needs or moderate social embeddedness. These findings highlight the potential role of AI-mediated interactions in supporting well-being and call for further research on causal mechanisms and responsible design to complement real-world social relationships.

## Association between handgrip strength and lung function by age and sex

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**Background :** The association between handgrip strength and lung function has been explored in previous studies, yet few studies have addressed how this relationship varies by sex and age in healthy populations. This study aimed to evaluate sex- and age-specific associations between handgrip strength and lung function in a healthy adult population.

**Methods :** This cross-sectional study included individuals undergoing health check-ups at a regional hospital in Japan. Collected information included handgrip strength, spirometry, and health-related lifestyles. Handgrip strength was assessed using a digital dynamometer. Multiple regression analyses were conducted to explore the relationship between handgrip strength and lung function parameters. Logistic regression analyses were used to estimate odds ratios (OR) and 95% confidence intervals (CI) for abnormal lung function per 5 kg increase in handgrip strength.

**Results :** A total of 1622 individuals were included in the study (age ranged 25-86 years). Linear regression analysis showed a positive association between handgrip strength and FEV1, percentage of the predicted FEV1 value (FEV1% predicted), FVC, and percentage of the predicted FVC value (FVC% predicted) across all age groups in women ( $p < 0.05$ ). In men, these associations were significant in the 25-44- and 45-59-year age groups ( $p < 0.05$ ). Logistic regression indicated that a 5 kg increase in handgrip strength was significantly associated with reduced abnormal lung function in both men (OR=0.790, 95% CI=0.673-0.927;  $p < 0.01$ ) and women (OR=0.598, 95% CI=0.461-0.775;  $p < 0.01$ ).

**Conclusion :** Handgrip strength is positively associated with FEV1 and FVC, both in absolute and predicted percentage values, across all age groups in women and in men under 60 years of age. Handgrip strength measurements integrated into regular health checkups may help in the early detection of lung function abnormalities.

## The epidemiology of esophageal cancer in high-incidence and non-high-incidence areas of North China

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**Background :** To analyze the trends of esophageal cancer in high-incidence and non-high-incidence areas of North China firstly.

**Methods :** All new cases of esophageal cancer in 2011-2021 from 45 cancer registries in Hebei Province were collected. Cixian and Shexian were regarded as high-incidence areas of esophageal cancer. The data were pooled and analyzed, and the crude rate and the standardized rate of different regions, period, sex and age were calculated.

**Results :** The incidence rate of esophageal cancer in high-incidence areas was higher 4.53 times than that in non-high-incidence areas. The mortality rate of esophageal cancer was higher 5.27 times. In North China, middle third, lower third, upper third and overlapping cancers accounted for 66.04%, 16.75%, 12.03% and 5.19%, respectively. In high-incidence areas, they accounted for 23.82%, 4.03%, 62.17% and 9.98%, while in non-high-incidence areas they accounted for 66.58%, 13.28%, 13.98% and 6.16%. Squamous cell carcinoma was the most common histological type, accounting for 88.67%, while they accounted for 99.05% and 68.22% in the high and non-high areas. In high-incidence areas the ASIRW was decreased from 2011 to 2021 with the AAPC of -4.6% (95CI: -5.7~-3.6), while in non-high-incidence areas it was decreased with the AAPC of -8.5% (95CI: -10.1~-6.8). In high-incidence areas of North China the ASMRW was decreased with the AAPC of -4.0% (95CI: -5.1~-2.8), while in non-high-incidence areas it was decreased with the AAPC of -6.3% (95CI: -9.5~-3.1).

**Conclusions :** The incidence and mortality rates of esophageal cancer in North China have shown a significant downward trend. Among them, the decline in non-high-incidence areas was more significant than that in high-incidence areas. Reducing the incidence and mortality rates of esophageal cancer in North China, especially in high-incidence areas, is a long and arduous task.

## Association between Good-Quality Sleep and Thyroid Peroxidase Antibody Positivity

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**Background :** Because low sleep quality induces inflammation, good-quality sleep might have a beneficial influence on suppressing inflammation. Since thyroid peroxidase antibody (TPO-Ab) positivity has been reported to be positively associated with inflammatory activity known as autoimmune thyroiditis, good-quality sleep could be inversely associated with TPO-Ab positivity. However, the beneficial influence of good-quality sleep on the status of TPO-Ab is unknown.

**Methods :** To clarify the association between TPO-Ab positivity and good quality sleep, a cross-sectional study with 1,324 euthyroid participants (free triiodothyronine [T3] and free thyroxine [T4] were within normal values) was conducted. If the participants replied “yes” to the question “Are you getting enough rest by sleep?”, they were deemed to have good-quality sleep.

**Results :** Among the study population, 242 participants had TPO-Ab positivity and 993 had good-quality sleep. Good-quality sleep is revealed to be inversely associated with TPO-Ab positivity. The sex and age-adjusted odds ratio (OR) (95% confidence intervals [CIs]) of TPO-Ab positivity for good-quality sleep was 0.68 (0.50, 0.92). Even after further adjustment for free T4, thyroid stimulating hormone, mental distress, high body mass index [BMI] ( $\geq 25.0 \text{ kg/m}^2$ ), low BMI ( $< 18.5 \text{ kg/m}^2$ ), current drinking status, current smoking status, and exercise, the association remained significant. The adjusted OR (95% CIs) was 0.66 (0.48, 0.90).

**Conclusion :** Among the euthyroid population, an inverse association between TPO-Ab positivity and good-quality sleep was observed. Even further investigation of longitudinal studies is necessary; good-quality sleep might prevent autoimmune thyroiditis because TPO-Ab positivity is a known pathogenesis factor of autoimmune thyroiditis.