Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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several studies conducted by Tools4Patient. These chronic pain patients were suffering from peripheral neuropathic pain or painful osteoarthritis of the knee and hip. They received a blinded placebo (oral, BID) for a duration varying from 1 to 3 months. The primary endpoint was the change from baseline of the weekly mean of the daily average pain score (APS). The placebo response, as measured by the primary endpoint, was modeled using a gaussian process with a linear kernel. In the current trial conducted by UNITY, the model predicted the placebo response for each patient and each endpoint using only data available at baseline.

**Testing the performance of the model**

The predictive performance of the model was tested both in the placebo group and the per-protocol population. The performance was evaluated with the Pearson’s correlation between the predicted placebo response and the actual observed response. The R-squared was also reported and represents the diminution of the variance of the estimated treatment effect. Higher R-squared values mean better estimation of treatment effect and increased study power. The model’s predictions were performed at baseline and could be considered as a baseline covariate under the EMA and FDA guidances for the use of baseline covariates. For the estimation of the treatment effect, we used this predicted baseline placebo covariate as any other typical covariate in an ANCOVA analysis. This adjusted analysis corrected for the range of placebo responsiveness in all trial patients.

**Results:**

**Results of UNITY study**

Strong placebo response was observed right after the injection that reached a plateau after 8 weeks. There was no statistically significant difference between any arm of UBX101 and placebo at the 12-week endpoint for change from baseline in WOMAC-Pain (primary endpoint).

**Results in prediction**

Table 1 presents Pearson’s correlations between the predicted placebo response and the observed responses in the placebo group. The predictions are highly statistically significant for all primary and secondary endpoints. The correlations were excellent and ranged between 45.8% and 59.7%. In particular, the model could explain 35.6% of the variance related to the placebo response of the primary endpoint (WOMAC-Pain). The model was also tested on all patients from the per-protocol population (N=173). The performance (Table 2) was also highly significant with all p-values below 0.001. The predictive placebo response model was able to explain 27.7% of the WOMAC-Pain response. Those Results were consistent across time points with excellent results until end-of-treatment (24 weeks).

**Placebell adjusted estimation of the treatment effect**

This predicted placebo covariate was used in the estimation of the treatment effect. We observed a 40% increased in the precision of the estimated treatment effect. These analyses adjusted for the predicted placebo response further confirmed the lack of efficacy of the UBX101 treatment in painful knee OA. In particular, we were able to show that the small differences observed between the treatment groups could, in part, be explained by slight imbalances in placebo response.

**Conclusions:** Tools4Patient has developed a machine learning model able to predict the placebo response in chronic pain RCTs. This model, named Placebell, was used in a phase II, randomized clinical trial conducted by UNITY Biotechnology investigating the effect of an intra-articular injection in approximately 180 patients suffering from painful osteoarthritis of the knee. The model predictions were highly significant for all primary and secondary endpoint (p<0.001). In particular, the model explained 27.7% of the primary endpoint (WOMAC-Pain) variance in the per-protocol population. Similar performance was also observed for the secondary time points confirming the robustness of the Placebell model. The Results also demonstrate its applicability in RCTs with different modes of administration (oral vs. Intra-articular injection).

We have also shown how this machine learning model could be used to improve the estimation of the treatment effect. Indeed, using the predictions as a covariate significantly reduced the variance resulting in a 40% increase in precision of the treatment effect. This gain in study power by increasing precision is exactly similar to that one would achieve by increasing sample size by 40% (here 72 additional patients).

Overall, the current Results further demonstrate the usability and performance of Tools4Patient’s placebo response model. Its excellent results across two indications, two modes of administration, and several endpoints raise the hope for wide applicability of this approach in pain indications.

**PRESENTATION NUMBER: LBA-27\n**

**IMPACT OF COVID-19 PANDEMIC ON PHYSICAL ACTIVITY, PAIN, MOOD, AND SLEEP IN ADULTS WITH KNEE OSTEOARTHRITIS**

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**Purpose:** The COVID-19 pandemic has significantly disrupted people’s daily lives. Restrictions on mobility and social interactions as well as reduced access to healthcare due to COVID-19 could have affected physical activity and symptomatology in people with knee osteoarthritis (OA). The purpose of this study was to leverage an ongoing randomized clinical trial (RCT) to examine the changes in physical activity, knee pain, mood, and sleep in people with knee OA during the ongoing COVID-19 pandemic.

**Methods:** Data were analyzed from participants recruited from the Greater Boston Area with symptomatic knee OA (n=28) enrolled in a parallel two-arm RCT (NCT03064139). Inclusion criteria were age between 50-80 years, BMI ≤ 40 kg/m², knee pain ≥ 4 on 0-10 numeric scale, meet the American College of Rheumatology clinical criteria for knee OA, own a smartphone, and able to walk for 20 minutes without assistance. Exclusion criteria were contraindications to exercise, use of orthotics for knee pain, knee injections in the previous 3 months, current receiving physical therapy for knee pain, planning major treatment for knee pain in next 6 months, history of joint replacement, and major inflammatory, neurologic, or muscular conditions. Participants were assigned to either a mindful walking or self-management group. The intervention for both groups was paused upon the declaration of the COVID-19 pandemic. However, participants continued to wear a wrist-worn activity monitor (Charge 3, Fitbit, San Francisco, CA, USA) and complete weekly surveys remotely. The activity monitor was used to extract daily step count and sleep duration. Activity data were only considered valid if they pertained to a day with ≥10 waking hours of wear time. Weekly surveys were used to report knee pain (no pain to worst imaginable), positive mood (neutral to happy), and negative mood (neutral to sad) on a 0-10 numeric scale. For these metrics, data were averaged first within each participant over a given time-period,
and then across all participants for that period. Descriptive data are reported for three time periods: an 8-week baseline period from January 15 to March 10, a 10-week period from March 11 to May 19 when a stay-at-home advisory was in effect in the state of Massachusetts, and a 12-week period from May 20 to August 11 reflecting the phased reopening in the state of Massachusetts.

**Results:** Participant characteristics are shown in Table 1. As shown in Table 2, when averaged across all participants, small changes with unclear clinical significance were seen during the stay-at-home advisory and reopening phases compared to the baseline for all outcomes. Specifically, a slight decrease in physical activity, increase in sleep duration, and worsening of positive and negative mood was seen during the initial stay-at-home advisory period with some recovery towards baseline values during the reopening periods. Knee pain showed a slight improvement during the pandemic. However, substantial variability across the participants was evident in changes from the baseline values as shown in Figures 1 and 2.

**Conclusions:** In this urban cohort of people with knee OA, effects of the COVID-19 pandemic on physical activity, sleep, pain, and mood were variable across individuals. While some individuals were able to maintain or recover their physical activity to levels similar to those prior to the pandemic, many continued to show reduced activity many months into the pandemic. Similar variability was seen for sleep, pain, and mood outcomes as well. While reasons for this variability are not clear from this small sample, change in seasons, severity of stay-at-home restrictions across counties, employment types, the local built environment, and intervention groups are some of the external factors that may have influenced people’s behavior, in addition to psychological factors. Given the prevalence of knee OA, worsening of knee OA related outcomes even in a small proportion could have significant public health impact on the broader societal scale. Strategies are needed to identify individuals with knee OA who are exhibiting reduced physical activity and/or worse symptoms during the pandemic so that appropriate healthcare services can be targeted to these individuals.
ALLOSTATIC LOAD AND OSTEOARTHRITIS
A CROSS-SECTIONAL ANALYSIS OF THE RELATIONSHIP BETWEEN ALLOSTATIC LOAD AND OSTEOARTHRITIS

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Purpose: Metabolic influences and systemic low-grade inflammation are increasingly recognised in osteoarthritis (OA) development and pathophysiology. Cumulative stress-response system dysregulation, known as allostatic load (AL), has been suggested as a potential mechanism to explain relationships between social determinants (e.g. adverse childhood experiences) and arthritis but has not yet been explored with a primary outcome of OA. Measured using a composite index of clinical biomarkers to indicate physiological dysregulation, AL is associated with adverse health outcomes including cardiovascular disease, frailty and mortality. A better understanding of the potential cumulative, systemic physiological influences on OA development could improve primary OA prevention at a population level. The primary objective of this study was to conduct a preliminary investigation into the cross-sectional relationship between AL and the presence of OA in a population sample. Acknowledging the known limitations of self-reported disease data in population studies, we further explored the nature of the relationship based on different definitions of OA.

Methods: The North West Adelaide Health Study is a South Australian population-based cohort study of over 4000 individuals. This cross-sectional study used Stage Two (2004-2006) data from a clinic visit, computer-assisted telephone interview (CATI) and written questionnaire, as well as linked Pharmaceutical Benefits Scheme (PBS) medication data. The primary outcome, OA, was defined by self-report and medication data. During the CATI, participants were asked whether they had ever been told by a doctor that they had arthritis (yes; no) and, if so, what type they had (OA; rheumatoid arthritis (RA); other type of arthritis). Participants who reported an Other type of arthritis were excluded from all analyses. Additionally, participants who were dispensed disease-modifying anti-rheumatic drugs (DMARDs) during the Stage Two data collection period were excluded, due to a high likelihood of diagnosed inflammatory arthropathy. All other participants who self-reported arthritis were classified as having OA. The exposure variable, AL, was a composite index of nine biomarkers: systolic and diastolic blood pressure (SBP; DBP), waist-to-hip ratio (WHR), body mass index (BMI), total cholesterol (TC), high-density lipoprotein cholesterol (HDL), glycohaemoglobin (HbA1c), interleukin 6 (IL6) and tumour necrosis factor alpha (TNF-α).

Results: In unadjusted analysis, OA participants with DM reported poorer TUG test (β= 1.786 (0.520-3.053), p=0.006), poorer IADL (β= 0.275 (-0.499 - 0.051), p=0.016) and more anxiety (β= 1.172 (0.173-2.170) p=0.022). The associations observed were remained significant even after the adjustment of age, gender and BMI. No significant difference was found on pain severity, QoL, Depression and Stress level.

Conclusions: This study highlights the impact of DM on functional, physical and psychological level among OA older people and this was independent of age and BMI. Prevention of OA among DM patients and vice-versa are therefore warranted. This study emphasize the need to consider comorbidities in treating OA patients.

PRESENTATION NUMBER: LBA-29

IMPACT OF DIABETES MELLITUS ON PAIN, PHYSICAL PERFORMANCE, PSYCHOLOGICAL STATUS AND QUALITY OF LIFE IN OSTEOARTHRITIC OLDER PEOPLE LIVING IN LOW AND MIDDLE-INCOME NATION RESULTS FROM MALAYSIAN ELDERS LONGITUDINAL STUDY

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Purpose: To determine the impact of Diabetes Mellitus (DM) on physical performance, psychological status and quality of life in knee osteoarthritic (OA) older people.

Methods: This is cross-sectional analysis from first wave data of Malaysian Elders Longitudinal Study. We included 402 knee OA individuals, 234 with DM [mean (SD) age=69.21 (7.49)] and 168 [mean (SD) age=68.91 (7.46)] without DM. Participants was asked to rate the severity of pain either as mild, moderate or severe. Physical and functional performance were measured using the Timed Up and Go test (TUG) and the Katz and Lawton scales respectively. Psychological status was determined using the Depression Anxiety and Stress Scale (DASS-21). While, Quality of life (QoL) was determined using CASP19.

Results: In unadjusted analysis, OA participants with DM reported poorer TUG test (β=1.786 (0.520- 3.053), p=0.006), poorer IADL (β=0.275 (-0.499 - 0.051), p=0.016) and more anxiety (β=1.172 (0.173-2.170) p=0.022). The associations observed were remained significant even after the adjustment of age, gender and BMI.

Conclusions: This study emphasizes the need to consider comorbidities in OA treatment.

PRESENTATION NUMBER: LBA-29

RESULTS FROM MALAYSIAN ELDERS LONGITUDINAL STUDY
OLDER PEOPLE LIVING IN LOW AND MIDDLE-INCOME NATION PSYCHOLOGICAL STATUS AND QUALITY OF LIFE IN OSTEOARTHRITIC IMPACT OF DIABETES MELLITUS ON PAIN, PHYSICAL PERFORMANCE, CURRENT NUMBER: LBA-28

Figure 2 Change from baseline in knee pain (TOP), positive mood (MIDDLE), and negative mood (BOTTOM) during stay-at-home and reopening time-periods compared to baseline for each participant (colored lines) and overall cohort (dotted black line). Note that mean value (empty circle) is differs slightly from that in Table 2 due to missing data for some participants in Phases 1 and 2.