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# U Ottawa Faculté de Médicine Faculty of Medicine

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# Prediction Models for the Prognosis of Recurrent Stroke in Patients with TIA and Minor Stroke: A Systematic Review of Methodologic Quality of Derivation and Validation Studies

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### **ABSTRACT**

**Introduction:** Stroke is a common and serious disorder that often leads to death and disability. It is preventable with one of the most serious risk factors being a prior transient ischemic attack (TIA) or minor stroke. Clinical prediction models are increasingly used to identify TIA patients to determine their subsequent stroke risk. While several clinical prediction models exist, their derivation and validation methodological quality is unknown. In this systematic review we aim to appraise the methodological quality of the derivation and validation of the available models.

**Methods:** This systematic review followed an adapted version of TRIPOD and CHARMS guidelines. Medline and Embase databases were searched up to February 04, 2020 with the help of two experienced medical librarians. Studies reporting development or validation of multivariable prognostic models predicting recurrent stroke within 90 days in patients with TIA or minor stroke were included. Review articles, non-English, diagnostic, or predictor finding studies (exploring association of predictors with outcome) were excluded. Included models were appraised for methodological quality by reviewing their reporting and study conduct.

Results: After screening 7026 articles, 60 eligible articles were retained: two were prediction model development with external validation, two were prediction model development without external validation, 16 were external model validation with model updating and 40 were external model validation without model updating studies. All studies were published between 2000 and 2020. Data were extracted on 100 different derivations and validations. Sixty cohorts used prospective data collection, 39 used retrospective and one was unclear. A descriptive title was provided for 25% of the studies while 66% had a clear rationale. Information on participants was not well reported with only 25% of the cohorts presenting essential demographic information for comparison between validation and derivation datasets. Recruitment method and study setting types were also poorly reported. Only 44% of the cohorts reported whether the same outcome definition was used for all patients with only 24% of the cohorts reporting blinding of the outcome. Blinding of predictors was rarely (12%) assessed or reported with limited information on timing and method for measuring predictors. Sample size justification was provided for only about half of the cohorts. Missing data were rarely reported (28%) and handled (22%). Performance measurements were poorly reported with only 5% of the cohorts having information on calibration. Of the derivation and updating models, just 4% reported applying shrinkage. Of the updated models, only 9% followed recommended methods to apply less extensive methods first.

**Conclusions:** The vast majority of prediction models for the prognosis of recurrent stroke in TIA and minor stroke patients suffer poor methodological quality in terms of reporting and conduct. We suggest that all prediction model development and validation follow the TRIPOD checklist, at a minimum.

## Risk assessment of the impact of Ministry Inspection changes on the first wave of COVID-19 in Ontario's Long-Term Care Homes

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### **ARSTRACT**

Introduction: The first wave of the COVID-19 pandemic disproportionately affected Long-Term Care Home (LTCH) residents in Ontario, Canada. From January 15 to June 1,2020, 75% of all COVID-19 related deaths in Ontario were in LTCH residents. Infection Prevention and Control (IPAC) practices are a key factor in reducing transmission and controlling outbreak, in particular the use of Personal Protective Equipment (PPE). Resident Quality inspections (RQIs) by the Ontario Ministry of Long-Term Care (MLTC) include inspection of the Home's IPAC program. The MLTC changed from an annual RQI framework to a risk-based inspection framework in fall 2018. The MLTC conducted fewer RQIs in 2019, as compared to the preceding four years. Advocates have called for investigation on how scaled-back IPAC inspection may have left Homes unprepared for the COVID-19 pandemic.

**Methods:** The U.S. Presidential/Congressional Framework for Environmental Health Risk Management was used to assess the risk of reduced MLTC inspections on the first wave of COVID-19, with a focus on IPAC/PPE programs, and to propose risk mitigation options.

Results: Data from RQI reports show that from June 2013 to January 2015, 67% of the 629 Homes inspected were cited for non-compliance in the IPAC Program. For the fiscal year 2017 to 2018, 63.3% of the 594 Homes inspected had IPAC non-compliance findings. In 2019, 27 out of 626 LTCH in Ontario received a RQI.

**Conclusions:** The reduction of RQIs in 2019 creates a knowledge gap and hinders baseline assessment of LTCH IPAC performance in the year prior to the pandemic. The IPAC risk issues can be managed by reinstating annual comprehensive inspections of every LTCH and requiring mandatory follow-up by inspectors on all IPAC findings. Home IPAC programs should be supported by increased funding for training and staff, and enhanced partnership with the establishment of a Long-Term Care unit in every Public Health Unit.

# Prenatal Maternal Stress, Offspring Internalizing and Externalizing Symptoms, and the Moderating Role of Parenting: Findings from the Norwegian Mother, Father, and Child Cohort Study (MoBa)

Clayborne, ZM<sup>1,2</sup>, Nilsen, W<sup>3</sup>, Torvik, FA<sup>2,4</sup>, Gustavson, K<sup>5,6</sup>, Bekkhus, M<sup>5</sup>, Gilman, SE<sup>7,8</sup>, Khandaker, G<sup>9,10,11,12</sup>, Fell, DB<sup>1,13</sup>, Colman, I<sup>1,2</sup>

### **ABSTRACT**

**Introduction:** Children exposed to maternal stress in utero are at greater risk of experiencing mental health problems later in development. However, few studies have examined how modifiable factors, including parenting, interact with prenatal maternal stress to influence later mental health. The aims of this study were to examine the associations between prenatal maternal stress and children's internalizing and externalizing symptoms at age 8, and to assess the moderating roles of sex and parenting behaviours on these associations.

**Methods:** The sample included 15,963 mother-child dyads from the Norwegian Mother, Father and Child Cohort Study (MoBa). A broad measure of prenatal maternal stress was constructed using 41 self-reported items measured at 17 and 30 weeks' gestation. Parenting measures were assessed by maternal report at child age 5, and included positive parenting, parental involvement, and inconsistent discipline. Child symptoms of internalizing and externalizing disorders were assessed by maternal report at age 8. Multiple group analyses were conducted to assess for sex-specific effects, and latent moderated structural equations were used to model interactions between prenatal maternal stress and parenting behaviours.

**Results:** Prenatal maternal stress was associated with child internalizing and externalizing symptoms; associations with externalizing symptoms differed by sex. Strength of associations between prenatal maternal stress and child depression, and conduct disorder and oppositional defiant disorder in male children, increased as levels of inconsistent discipline increased. Strength of the association between prenatal maternal stress and symptoms of attention-deficit hyperactivity disorder in female children was attenuated as levels of parental involvement increased.

**Conclusions:** This study confirms associations between prenatal maternal stress and offspring mental health and behaviour, and further suggests that these associations may be modified by parenting behaviours in early childhood. Findings can help inform the development of public health strategies to support maternal-child mental health and wellbeing and improve children's life chances.

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# Comparative Analysis of SARS-CoV-2 Diagnosis Specificity and Sensitivity Using Three Sampling Methods by Quantitative PCR and Droplet Digital PCR

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### **ABSTRACT**

**Objectives:** Limitations of nasopharyngeal (NP) collection for SARS-CoV-2 diagnosis include patient discomfort, need for professional collection, and supply shortages. Saliva and oropharyngeal (OP) sample collection have been found to be reliable alternatives, with potential to improve test compliance and facilitate population-level testing. Here we performed a prospective diagnostic accuracy study using NP, OP, and saliva samples from 20 SARS-CoV-2 positive cases.

Methods: NP, OP, and saliva samples were collected from 20 adults with recent positive SARS-Cov-2 NAAT test, and ≤ 10 days symptom onset or positive test date, whichever first. Saliva was collected using the OMNIgene•ORAL (OM-505) Kit [DNA Genotek]. Negative controls were collected from 10 asymptomatic adults. Viral RNA was extracted using a QIAamp Viral RNA Mini Kit [Qiagen, 52906]. Quantification cycle (Cq) values (qPCR) and genomic equivalent copy number determination (ddPCR) were performed for SARS-CoV-2 (Wuhan) N1 and E genes and the RPP30 internal control.

**Results:** ddPCR yielded one (1/10) false positive NP swab. qPCR and ddPCR results were otherwise accurate for all positive and negative NP, OP, and saliva samples. 100% sensitivity was achieved for saliva samples using both quantification methods. While NP and saliva copy numbers and Cq values were comparable, N1 and E target gene amplification were approximately 100-fold less efficient for OP swabs. Detection of N1 demonstrated slightly higher sensitivity than the viral E gene.

Conclusion: Saliva vRNA detection sensitivity was comparable to NP sensitivity, and superior to OP sensitivity. These results support the use of saliva in widespread SARS-CoV-2 testing and for population-scale epidemiological studies. Early morning collection may have favorably contributed to the performance of saliva testing. Going forward, 1) These collection strategies will be evaluated in an automated and high throughput RNA extraction system, and 2) NP, OP, and saliva viral titres will be compared and correlated to COVID-19 symptom severity.

### A Global Assessment of Patient Engagement in Preclinical Laboratory Research

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### **ABSTRACT**

Introduction: 'Patient engagement' strives to co-create research with patients and the public and has been observed to align research with the priorities of the ultimate end user. Although patient engagement within clinical research has been well documented, the prevalence and effects of patient engagement in preclinical research (i.e. research conducted in cell and animal models in a laboratory-based environment) remain unclear. The aim of this review is to systematically identify reports of patient engagement in preclinical laboratory research and identify benefits, barriers, and enablers to engagement.

**Methods:** MEDLINE, Embase and grey literature sources (Google, ProQuest) were systematically searched. Records were independently screened by two reviewers. Primary studies and review articles that described or investigated patient engagement in preclinical laboratory research were included. Patient engagement activities where patients (i.e. patients, family members, care givers or community members) provided input, guidance, or consultation on at least one element of the research process were eligible for inclusion. Study characteristics and outcomes were extracted and organized thematically. The International Association of Public Participation spectrum was used to categorize the level of engagement.

**Results:** 2,959 abstracts were screened, and 25 original studies were included (including 9 in vitro, and 8 in vivo studies). Studies were published between 2007 and 2019, with the majority of studies originating from the USA (n=8) and UK (n=8). Most studies engaged patients at the education or priority setting stages (n=21). Seven studies engaged patient partners at the empowerment level where patients were the ultimate decision makers. The most frequently reported benefit of patient engagement was 'providing a mutual learning opportunity', which allowed researchers to see the real-life implications of their work and stimulate patient partner interest in preclinical laboratory research. Reported barriers to patient engagement reflected concerns around 'differences in knowledge and research experience' and how this may limit meaningful patient engagement and challenge communication. The most commonly reported enabler was 'creating engagement activities and environments where team members felt comfortable sharing individual views'.

**Conclusions:** Our scoping review identified examples of patient engagement across several stages of preclinical research and at each level of engagement. These results will be used to create a comprehensive framework to facilitate future patient engagement in preclinical research.

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### The Gendered Relationship Between Illicit Substance Use and Self-Harm in Norwegian Students Pursuing Higher Education

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### **ABSTRACT**

**Background:** Young adults have some of the highest rates of self-harm and substance use. Compared to suicidality, non-suicidal self-harm has received less attention, and the role of gender is inconclusive. Using a large epidemiological student survey, we sought to examine the potentially gendered relationship between substance use and self-harm.

**Methods:** 50,054 full-time Norwegian students (18-35 years) completed a survey (SHoT Study [2018]), including questions on past-year self-harm: non-suicidal thoughts of self-harm, non-suicidal self-harm, suicidal thoughts, and suicide attempt. Students reported past-year alcohol and illicit substance consumption, and perceived risk of cannabis use. Screening tools measured problematic alcohol and cannabis consumption. We used logistic regression modeling adjusted for age, symptoms of depression and anxiety, and financial hardship.

**Results:** Frequent alcohol consumption was associated with all outcomes, with the magnitude of most associations more than a two-fold increased likelihood of self-harm. Problematic alcohol consumption was associated with nearly all outcomes: odds ranging from 1.09 (95%CI:1.01,1.18) for suicidal thoughts to 1.33 (95%CI:1.00,1.77) for suicide attempt. There was evidence of multiple illicit substance by gender interactions. Consumption of nearly all illicit substances was associated with self-harm for women. Women who perceived cannabis use as a health risk were more likely to experience non-suicidal thoughts as cannabis consumption increased, and with harmful consumption patterns. Associations between substance use and outcomes among men were inconsistent.

**Conclusions:** Alcohol consumption is associated with increased risk of self-harm and suicidality; however, associations between illicit substance use and self-harm and suicidality appear to be stronger in women compared to men.

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### **Cochrane 'Living' Systematic Review on Diagnostic Accuracy of Imaging For COVID-19: Update 2**

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### ABSTRACT

**Introduction:** The coronavirus disease 2019 (COVID-19) presents diagnostic evaluation challenges, including uncertainty regarding the diagnostic value of imaging tests. This is the second update of a 'living' systematic review, which aims to evaluate the diagnostic accuracy of chest imaging (computed tomography (CT), X-ray and ultrasound) in individuals with suspected COVID-19.

**Methods:** The Bern COVID-19 Living Database, Cochrane COVID-19 Register, and CDC Library were searched through 30/9/2020. Diagnostic accuracy studies involving participants with suspected COVID-19 were included. Screening, data extraction, and risk of bias assessments (QUADAS-2) were completed independently, in duplicate. Pooled accuracy estimates and 95% confidence intervals (CI) were determined using a bivariate random effects model. Meta-regression was used to compare modalities and investigate sources of heterogeneity.

Results: Fifty-one studies (19775 participants, 10155 (51%) cases) were included; the reference standard was reverse transcriptase polymerase chain reaction (RT-PCR) in all studies. Risk of bias concerning: participant selection was high in 10 (20%) and unclear in 22 (44%) studies; reference standard was high in 20 (39%) and unclear in 20 (39%) studies. Chest CT (41 studies, 16133 participants) had pooled: sensitivity=87.9% (95%CI 84.6-90.6); specificity=80.0% (74.9-84.3). Chest X-ray (9 studies, 3694 participants) had pooled: sensitivity=80.6% (69.1-88.6); specificity=71.5% (59.8-80.8). Ultrasound (5 studies, 446 participants) had pooled: sensitivity=86.4% (72.7-93.9); specificity=54.6% (35.3-72.6). Chest CT, X-ray and ultrasound had similar sensitivities (p≥0.05). Chest CT had a higher specificity (p=0.014) than ultrasound; chest X-ray had similar specificities compared to chest CT and ultrasound (p≥0.05). Reference standard and index test positivity were not identified as sources of heterogeneity for sensitivity or specificity (p≥0.05).

**Conclusions:** Chest CT is sensitive and moderately specific for diagnosing individuals with suspected COVID-19. Chest X-ray is moderately sensitive and moderately specific. Ultrasound is sensitive, but not specific. Chest CT and ultrasound may be useful for ruling out COVID-19, but not for distinguishing COVID-19 from other illnesses. However, the high or unclear risk of bias of included studies limits confidence in these findings.

**Disclaimer:** This abstract has been condensed from the Cochrane systematic review titled "Thoracic imaging tests for the diagnosis of COVID-19 [update 2]" (Islam 2020), which is licensed under CC BY-NC 4.0: www.creativecommons.org/licenses/by-nc/4.0/.

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### **BCG Vaccine Policies and Practices: Tracking Changes in National Policies in the BCG World Atlas**

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### **ABSTRACT**

**Introduction:** Although effective at preventing severe forms of childhood tuberculosis (TB), the bacille Calmette-Guérin (BCG) vaccine effectiveness is highly variable in adults. As a result, BCG vaccine policies and practices vary greatly across regions and have changed over the last few decades, along with global TB epidemiology. In 2011, the BCG World Atlas was launched as a searchable online database of global BCG vaccination policies. Common national policies include vaccinating all neonates, only defined high-risk groups or no BCG vaccination. The aim of this study is to explore whether changes to national BCG vaccine policies between 2009-2019 are associated with countries' decreasing TB incidence over the same time period.

**Methods:** A data hackathon organized in April 2020 gathered new data about past and present BCG policies and the 3rd edition of the BCG Atlas was launched. Using this database, we identified countries who changed their national policy between 2009-2019. We graphed yearly TB incidence rates (IR) from WHO for each selected country according to year of policy change. A chi-square test (X2) was used to compare the difference in TB IR for each country, before and after the policy change. RESULTS: Out of 224 countries in the BCG Atlas, 11 changed their national policy between 2009-2019. The majority of countries (8/11, 72.3%) changed their national policy from providing BCG vaccination for all neonates to restricting BCG vaccination to specific high-risk groups only. With the exception of Spain, The X2 test showed no significant association between this policy change and TB IR over time. However, when looking at the graph, most of these European countries have a general decreasing trend for TB IR beginning from the year of policy change.

**Conclusion:** Several countries have moved from nationwide BCG vaccination to selected vaccination. Tracking these changes to national BCG policies and understanding the reasoning is helpful to policymakers and vaccine developers.

## The Effects of Interpregnancy Weight Change and Interpregnancy Interval on Gestational Diabetes Mellitus Recurrence

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### **ABSTRACT**

**Introduction:** Interpregnancy weight change and interpregnancy interval are important modifiable risk factors of gestational diabetes mellitus (GDM) recurrence at subsequent pregnancies. However, their combined effect on GDM recurrence is not clear. Our study aims to explore the independent and combined effect of these two factors on GDM recurrence.

**Methods:** We conducted a population-based retrospective longitudinal cohort study using Ontario birth registry data. Women were included if they had GDM at index pregnancy, received prenatal screening and gave two consecutive, singleton deliveries in Ontario during 2012-2019. Modified Poisson regression models were used to estimate the adjusted relative risks (RRs) and 95% confidence intervals (Cls) for GDM recurrence at the second pregnancy. The combined and interaction effects of the two exposures were assessed.

Results: Among 6,914 eligible women with GDM history, 3,713 (53.7%) had GDM recurrence in their second pregnancy. Compared to stable interpregnancy weight change (body mass index [BMI] change <1 kg/m2), weight gain (BMI increase ≥1 kg/m2) increased the risk of GDM recurrence (aRR 1.13, 95% CI [1.07, 1.18]) whereas weight loss (BMI reduce ≥1 kg/m2) decreased the risk (aRR 0.88, 95% [0.82, 0.95]). Interpregnancy interval ≥24 months was associated with an increased risk of GDM recurrence (aRR 1.07, 95% CI [1.02, 1.12]), compared to 12-24 months interval. Interpregnancy weight gain and long interval had sub-additive interaction on GDM recurrence (relative excess risk due to interaction (RERI)=-0.13, 95% CI [-0.20, -0.06]). Women with both interpregnancy weight gain and interval ≥24 months had 1.22 times risk of GDM recurrence (aRR=1.22, 95% CI [1.13, 1.33]).

**Conclusion:** Interpregnancy weight change and interpregnancy interval were independently associated with GDM recurrence. Weight gain and more than 24 months between pregnancies had an antagonistic effect on GDM recurrence. Interpregnancy care should be targeted for GDM women to minimize subsequent GDM recurrence.

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# Investigating the Role of Community Health Workers in Providing Health Services to those Impacted by Extreme Weather Events in Low- and Middle-Income Countries: A Systematic Scoping Review

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### **ARSTRACT**

Introduction: Extreme Weather Events (EWEs) have devastating economic and health impacts. In LMICS, they exacerbate pre-existing disparities and increase present vulnerabilities. The WHO states that community health workers (CHWs) are essential to mitigating gaps that exist in health systems of countries with an unequal distribution of and/or unanticipated need of healthcare resources. CHWs can be utilized to build resilience and meet health demands arising from natural disasters such as EWEs. This systematic scoping review looks to summarize the peer-reviewed and grey literature outlining the roles of CHWs in supporting those impacted by EWEs.

**Methods:** The PRISMA-ScR checklist was followed for conducting and reporting the review. The search strategy was composed of two components: CHWs and EWEs. The CHWs search component included terms, chosen from journal articles, that described CHWs or professionals with similar roles. The EWEs search component included terms describing weather extremes and events that would be classified as an EWEs per the set definition for the review.

**Results:** Thirty-four publications were selected for the review. The countries in the South-East Asia region were of focus most times by the publications. The review of the publications indicated that CHWs provided health services that focused predominantly on disaster response, mental health, and child health. Many publications covered the training that CHWs and community members received to help populations suffering from the impacts of EWEs. CHWs were portrayed in a positive lens with most publications highlighting the important roles they play in supporting their communities.

**Conclusion:** CHW and community responses to EWEs are reactive in providing support to vulnerable population with many publications outlining disaster preparation and planning steps, post-disaster. Mental health support services were integral to disaster preparedness with training being provided to CHWs as a reactive response to EWEs. The sporadic nature of EWEs requires further training of CHWs and community members that are disproportionately prone to natural disasters.

## A Cost-Utility Analysis of the Impact of Electronic Nicotine Device Systems on Health Care Costs and Outcomes in Canada

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### **ABSTRACT**

**Background:** Cigarette smoking is the most common cause of preventable disease and mortality in Canada. While Electronic Nicotine Device Systems (ENDS) are marketed as smoking cessation tools, there is evidence that they result in increased smoking initiation in individuals under age 25. We developed a Markov model to determine the impact of ENDS on life expectancy, quality adjusted life expectancy and smoking related health care costs in Canada.

Methods: We used gender-specific Markov models to examine smoking behaviours of non-smokers, current, and former smokers in relation to ENDS, as well as the impact of ENDS on mortality and smoking-related illnesses in cohorts of males and females aged 15-19. We estimated lifetime life years, quality-adjusted life years (QALYs) and smoking related health care costs from the perspective of a publicly health care system, in scenarios where i) ENDS are available (status quo), ii) ENDS are completely unavailable, and iii) ENDS are available for smoking cessation through health care provider prescription. A lifetime horizon was used. We used data from population-based surveys of the Canadian population where possible, and supplemented with data available through literature review. Analysis incorporated both positive and negative impacts of ENDS use: an increased risk of smoking imitation in non-smoking ENDS users and an increase in smoking cessation with smokers trying to quit.

**Results:** Outcomes are expressed per 1,000 individuals, and are based on expected values obtained through a Monte Carlo simulation of 10,000 replications. A discount rate of 1.5% was used. For males aged 15-19, life years, QALYs, and costs of smoking related diseases per 1000 individuals were 41,554, 35,871 and \$79,828,608.55 respectively, when ENDS were available; 41,569, 35,894, and \$79,827,013.62 when ENDS were unavailable, and 41,571, 35,897, and \$79,778,776.31 when ENDS were available through prescription only. For females, lifetime life years, QALYs, and costs of smoking related diseases per 1000 individuals were 43,595, 37,415, and \$69,431,666.50, respectively, when ENDS were available; 43,609, 37,436, and \$69,275,492.80 when ENDS were unavailable, and 43,610, 37,437, and \$69,265,836.90 when ENDS were available through prescription only. Thus, situations where ENDS are unavailable, or available through prescription only, are dominant over the status quo.

**Conclusion:** The results of this analysis show that, based on the assumptions outlined above, that a policy change whereby ENDS were unavailable to the Canadian population, or available through prescription only, are likely to increase population health and reduce health care costs.

### Improving the Health Equity of Women Now and in the Post COVID-19 Era: Mobile Technology Assisted Interventions for Pregnant and Postpartum Women

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### **ABSTRACT**

**Introduction:** Pregnant and postpartum women face major psychological stressors that increase their risk of developing common mental disorders, such as depression and anxiety, especially during the COVID-19 pandemic. Mobile interventions present a novel approach to prevent and manage these conditions. This equity-focused systematic review aimed to examine the effectiveness and equity impact of such interventions.

**Methods:** We systematically searched MEDLINE, EMBASE, and 4 other databases, from inception and until January 2021, for experimental studies that examined the impact of mobile interventions on the severity of common mental disorders, psychological stress, changes in the occurrence of common mental disorders, and utilization of mental and pregnancy related health care services. We used pooled and narrative synthesis methods, performed equity-specific analyses, critically appraised the methodological rigour of all studies, and assessed the certainty of findings using GRADE. We followed a collaborative research approach whereby knowledge users, including pregnant and postpartum women, were engaged in this work.

**Results:** Our search identified 6476 records, of which 18 randomized and non-randomized controlled trials were included for analysis. Our findings suggest that mobile interventions may prevent depression and reduce its severity throughout pregnancy and postpartum. Mobile cognitive behavioural therapy (CBT) was clinically effective in managing postpartum depression, whereas other interventions had no added benefit. Findings on psychological wellbeing showed potential, whereas anxiety and utilization outcomes were understudied. Benefits across different ethnicities suggest a solution to the health inequity of this population.

**Conclusions:** Novel mobile interventions show promise in preventing and managing common mental disorders among pregnant and postpartum women now and in the post COVID-19 era. More rigorous research that engages stakeholders in the co-creation of future research and development of mobile interventions is needed.

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### A Model to Predict Level of Prehabilitation Adherence in Older Adults with Frailty Having Cancer Surgery

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### **ABSTRACT**

**Background:** Frailty is a well-established predictor of adverse postoperative outcomes in older surgical patients and is especially common in older people having cancer surgery.1–4 Early evidence suggests exercise could improve postoperative outcomes for people with frailty;5 however, little is known about how to predict older people's engagement in exercise before surgery (i.e., prehabilitation) programs.

**Objective:** Our objective was to derive and validate a model to predict prehabilitation adherence in older adults living with frailty before cancer surgery.

**Methods:** This was a nested prospective cohort study of older adults with frailty having cancer surgery who participated in a randomized controlled trial of home-based prehabilitation. We developed a multivariable ordinary least squares linear regression model using pre-specified, prospectively collected covariates to predict adherence (% prescribed exercise sessions attempted). Our covariates (collected at baseline) were selected a priori based on clinical expertise and systematic review; they included age, sex, health-related quality of life, disability, frailty, previous physical activity, depression, and neoadjuvant therapy. Continuous variables were standardized and assessed for best fit using fractional polynomials. Optimism was estimated through internal validation using bootstrap validation.

**Results:** Ninety-five participants were included in the derivation set. Mean percent adherence was 60.9% (SD 34.0%). Previous physical activity and age were the only predictors found to be significant at the 5% level. The final model explained 26.8% of the variance in adherence, had a root mean square error (RMSE) of 31.3, and an optimism of 24.3%.

**Conclusions:** This model helps to explain a moderate degree of variation in prehabilitation adherence in older people with frailty, however, only two postulated factors were strong predictors individually. This model is an important first step toward personalizing prehabilitation support, but future research is needed to better understand predictors of prehabilitation adherence in older people with frailty.

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### **Examining the Effect of Maternal Pre-Pregnancy Body Mass Index on Allergic Disease Development** in Offspring: a Population-Based Study using Health **Administrative Databases in Ontario, Canada**

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### ABSTRACT

Introduction: Overweight and obesity are the most common pre-existing morbidities in pregnancy. Studies suggest excess pre-pregnancy weight may impact fetal immunological development through metabolic dysfunction and inflammation; however, little is known about its effect on pediatric allergic disease development. We sought to examine the effect of maternal pre-pregnancy body mass index (BMI) on incidence of four common allergic diseases in offspring.

Methods: We conducted a retrospective, population-based cohort study of all singleton live births in Ontario between 2012–2014, using maternalnewborn records from the provincial birth registry linked with health administrative databases. Neonates (N=248,017) were followed up to 7 years of age for diagnosis of asthma, rhinitis, anaphylaxis, and dermatitis, identified using validated algorithms based on diagnostic codes from healthcare encounters. Potential confounders were identified through directed acyclic graphs. Cox proportional-hazards models were employed to calculate adjusted hazard ratios (aHR), overall and stratified by infant sex to assess effect-measure modification.

Results: Records with missing data (60,073; 24.2%) were excluded from these initial analyses. Of the final sample, 10,221 (5.4%) infants were born to mothers who were underweight, 97,562 (51.9%) normal weight, 45.498 (24.2%) overweight, and 34.663 (18.4%) obese. Incidence rates (per 100,000 person-days) for anaphylaxis, asthma, dermatitis, and rhinitis were 0.21, 6.51, 12.01, and 1.53, respectively. Compared to normal weight, maternal obesity was associated with an increased hazard of asthma in offspring (aHR=1.08, 1.04-1.12), but a decreased hazard of anaphylaxis (aHR=0.77, 0.62-0.95). Maternal underweight was associated with an increased hazard of dermatitis in offspring (aHR=1.08, 1.03-1.13). Stratification revealed similar directions of associations by infant sex, though greater magnitudes for males.

Conclusions: Our findings suggest maternal pre-pregnancy BMI may have weak but important effects on pediatric allergic outcomes, particularly among male offspring.

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