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SYNERGISTIC EFFECT OF SENOLYTICS AND MECHANICAL LOADING ON TMJ CARTILAGE

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Objectives: The objective of this project was to determine if intermittent mechanical loading augments the beneficial effects of intermittent senolytics on temporomandibular joint(TMJ) cartilage in old age. Our hypothesis was that concurrent administration of senolytics and mechanical loading will have a synergistic anabolic effect on the cartilage of TMJ with aging. **Materials and Methods:** Using 18 month-old C57B6 mice(10 male and 10 female mice per group) treated for 4 months with either 1) vehicle (60% Phosal 50PG, 30% PEG-400, 10% Ethanol); 2) senolytics combination (Dasatinib: 5mg/kg body weight + Quercetin: 50mg/kg/day); 3) intermittent mechanical loading using the spring applying 50cN of compressive force one hour each day for 5 consecutive days; 4) senolytics treatment with intermittent mechanical loading; 5) D+Q with botox injection(0.3U, volume of 30ul) on the left side of masseter muscle. The condyle samples were harvested and examined with multiple approaches, including micro-CT analysis, histomorphometric analyses, immunostaining. **Results:** There was significant increased TRAP activity in D+Q with botox injection group. In Safranin O/Fast Green and Toluidine Blue staining, both intermittent D+Q and mechanical loading group improved cartilage integrity and cartilage thickness. Concurrent administration of D+Q and mechanical loading increased cartilage thickness more than D+Q and mechanical loading alone. There was significant decreased bone volume fraction in the botox group. **Conclusion:** Our results suggest that mechanical loading augments the beneficial effects of senolytics on the cartilage of TMJ in old age.

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N^4-(AMINO-SUBSTITUED)-*N*-SUBSTITUED-BENZENESULFONAMIDE SCAFFOLD TO DESIGN AND SYNTHESIZE NOVEL TREM-1 INHIBITORS AGAINST NEUROINFLAMMATION

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A neurological event, such as an ischemic stroke, causes defensive neuroinflammation, but it protracts neuroinflammation to a dangerously high level. Global ischemia is a severe form of stroke caused by heart arrest that affects 200,000 Americans each year and is associated with neurodegeneration and cognitive abnormalities. Current treatments aim primarily at alleviating symptoms rather than treating the condition. As a result, there is an unmet need for new targets for identifying novel molecules as a viable therapeutic for global ischemia induced neurodegeneration and cognitive deficits. The triggering receptor expressed on myeloid cells-1 (TREM-1), the immunoglobulin superfamily surface receptor primarily expressed on monocytes, macrophages, and neutrophils, has been found to be upregulated in the development of neuroinflammatory diseases, with inhibition providing protection. In our preliminary results from a global ischemia rat model, there is TREM1 upregulation at both mRNA and Protein levels in Post-ischemic hippocampal CA1 regions. TREM1 inhibition by known LR12 peptide and novel GJ079 molecule showed neuroprotection in ischemic insult. Thus, TREM1 inhibition can be a new therapeutic approach to treat Global ischemia. We identified *N*^{4}-(amino-substituted)-*N*-substitued-benzenesulfonamide scaffold molecule, GJ079 as a hit from molecular docking of 80K molecules in hTREM-1 (PDB: 1SMO) crystal structure. We verified GJ079 affinity to TREM1 by surface plasmon resonance (SPR) analysis with Kd = 14.3 uM. However, we witnessed some-solubility issue with GJ079. Notably, PLT137, a *fluro*-analog of GJ079 showed ~350 folds (Kd= 4.8 nm) affinity to TREM1 and better solubility. Thus, we hypothesized that *structural modifications in GJ079 molecule can develop non-toxic, bioavailable and potent TREM1 inhibitors*. We will test our hypothesis with following.

Aim: (A) To design structure activity relationship (SAR) of the GJ079 to develop its novel-analogs as palatable and potent TREM1 inhibitors with acceptable pharmacokinetic profile. (B) To evaluate *in vitro* pharmacological (high throughput assay, and IC_{50} determination) and Pharmacokinetic (solubility and toxicity) profiles of novel TREM1 inhibitors.

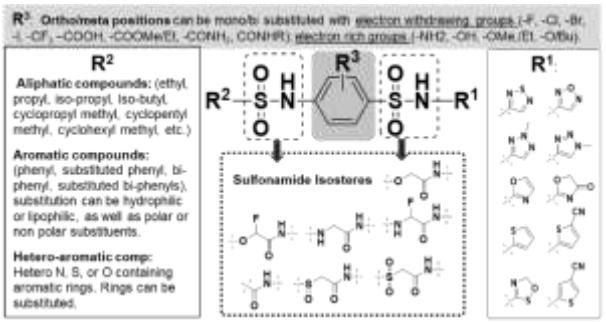

Fig 1 SAR development of GJ079- *N*^{4}-(amino-substituted)-*N*-substituted-benzenesulfonamide scaffold

A) Our findings revealed that the *para*-fluro alteration on the Phenyl ring of R^3 in GJ079 developed PLT134, which notably improve TREM1 affinity and solubility. As a result, the structure of GJ079 is amenable to chemical changes (Fig 1) to develop more potent analogs. We propose a two-pronged approach to advance **GJ0079** as initial hit-to-lead candidate. First is a structure guided approach to develop active pharmacophores for TREM1 inhibition in nanomole concentration and with good solubility. Second, is to improve pharmacokinetic profile and selectivity towards TREM1. We will use focused SAR tactics (Fig 1) to obtain ~200+ analogs of GJ079. First, we will substitute R^1 position with isostearic 5-membered heterocycles. Heterocycles can be substituted. Second, we will replace *sulfonamide(s)* group by isosteric amido, imido, or extended amino, 2-sulfoxide or 2-sulfone acetamides (dotted square). We will also place fluorine (F) on α-carbon to verify if keto-enol tautomerism is tolerated. We anticipate that extended sulfonamide isosteres will retain ligand's interaction with central and backbone residues in the binding pocket. We anticipate F with being electron deficient will lock analogs conformation into more stable and active tautomeric form. Third, we will substitute *phenyl* (R^3) with electrophilic, and electron deficient functions. We anticipate this will generate new polar interactions to increase potency. Finally, we will replace bulky group (R^2) with stereo equivalent aliphatic, aromatic or hetroaromatic substitutions. Aromatic or heteroaromic rings will be substituted with other pharmacophores.

B) We will employ SPR screens to quantify binding affinities (Kds) of analogs for TREM1 and eliminate non-binding analogs. We will determine analog toxicity (TC_{50}) using LDH assays in primary hippocampal cultures. We will employ TREM1/DAP12 promoters stably expressed in HEK293 cells with lacZ reporter gene high throughput screening (HTS) assay to determine TREM1 inhibitory potential. We will also determine in *vitro* inhibitory potency (IC_{50}) of analogs for TREM1. We anticipate identifying analogs with nanomole inhibitory activity. The top 2% most potent analogs will be assessed further by TREM1 downstream signaling molecules in primary hippocampal cultures.

Results and Conclusion: We successfully optimized a series of chemical reactions involving multi-step chemical synthesis. We have synthesized 14 molecules from N-substituted benzene sulfonamide series where, R^1 =thiazole. We have synthesized 21 molecules with substitutions at *N*^{4}-amino group. We have synthesized 3 molecules from third series with an aromatic substitution at R^2 position. Compounds were purified using flash chromatography, and their chemical integrity was confirmed using ^{1}H NMR and ^{13}C NMR and LCMS. In conclusion, PLT134 have shown improved solubility as well as ~350-fold increase of affinity to TREM 1 compared to GJ079. Currently we are developing *in vitro* cell assay to perform HTS for hit to lead optimization. In addition, pharmacokinetic profile analysis and SPR will be performed for potent TREM 1 inhibitors.

REPURPOSING VORTIOXETINE AND NICLOSAMIDE FOR H3K27M PEDIATRIC HIGH-GRADE GLIOMAS

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Background: Pediatric gliomas are understudied and have been shown to harbor distinct genetic and molecular characteristics different from their adult counterparts. Due to this, the molecular mechanisms underlying pediatric high-grade glioma (pHGG) pathogenesis have yet to be fully elucidated, resulting in ineffective treatments and a lack of molecularly targeted pharmacotherapies. Various lines of evidence have pointed to epigenomic alterations of histone 3 lysine27-to-methionine (H3K27M) mutations as a key contributor to the development of the pHGG, diffuse intrinsic pontine glioma (DIPG). Additionally, it has been demonstrated that H3K27M mutations cooperate with *PDGFRA* mutations to accelerate glioma formation. Since H3K27M and PDGFRA are two of the most frequently mutated genes in pHGGs, they hold strong potential as therapeutic molecular targets.

Significance of Problem: pHGGs are aggressive primary malignant brain tumors in children and the leading cause of cancer-related deaths in young patients. With the current standard of care, <5% of patients survive five years after diagnosis, warranting an urgent need for novel targeted therapies.

Hypothesis: Vortioxetine and niclosamide will inhibit cell proliferation and growth of H3K27M mutant line SF8628 in vitro by inhibiting PI3K/AKT signaling pathways downstream from PDGFRA. Accordingly, these two drugs may be repurposed as novel pharmacotherapies for the treatment of H3K27M pHGGs.

Experimental Design: Using the integrated Library of Integrated Network-Based Cellular Signatures (iLINCS), a widely used bioinformatics platform, we identified potential therapeutic agents for drug repurposing based on the strength of their negative concordance with H3K27M pHGG cell signatures. Our preliminary results of iLINCS analysis suggested vortioxetine and niclosamide as top candidates. We selected both drugs due to their ability to inhibit the PI3K/AKT signaling pathway downstream of PDGFRA, frequently mutated in H3K27M pHGGs. We evaluated in vitro drug efficacy of vortioxetine and niclosamide on H3K27M tumor cells. To assess cell viability, we conducted MTT and colony formation assays. Furthermore, apoptotic and antiproliferation markers were evaluated through Western blotting.

Results/Data: Toxicity analysis demonstrated that vortioxetine, a commonly prescribed antidepressant, and niclosamide, an antihelminthic drug, are toxic to H3K27M patient-derived DIPG cells (SF8628), but not to non-transformed human astrocytes at their IC50 concentration. Vortioxetine effectively lowered cell proliferation and the ability to form colonies in H3K27M DIPG cells. On immunoblot analysis, vortioxetine's apoptotic and antiproliferative abilities were shown through increased cleaved PARP and caspase activation along with decreased ERK activation. Additionally, we found that niclosamide decreased DIPG cell viability in proliferation assays and induced apoptosis through increased cleaved PARP and caspase activation on Western blots.

Conclusions: Altogether, results showed that both drugs suppress H3K27M cell proliferation. These results support the repurposing of vortioxetine and niclosamide as promising potential therapies for H3K27M gliomas, and further studies are warranted in glioma xenograft models.

EXPANDING PROTAC SCOPE WHILE TARGETING FBXO21 FOR AML TREATMENT

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Proteolysis-targeting chimera (PROTAC) is an innovative approach in cancer research that uses the cellular ubiquitin-dependent proteolysis system for the efficient degradation of specific proteins.

While a majority of developed PROTACs have been limited to CRBN or VHL among the plethora of E3 ligases, this study explores alternative E3 ligases, particularly FBXO21, aiming to discover novel ligands that maximize the scope of PROTACs. Investigating FBXO21 stems from its overexpression in Acute Myeloid Leukemia which correlates with a significantly worse prognosis.

We hypothesize that directing PROTACs towards over-expressed E3 ligases associated with cancer aims to broaden their therapeutic window.

In this study, we first used a structure-based drug design (SBDD) approach to identify a potent ligand for FBXO21, a substrate recognition component of the Skp1-Cullin-F-box (SCF)-type E3 ligase complex. Using Schrödinger's GLIDE, we docked an FBXO21 substrate (EID1)-derived helical peptide into the alpha fold FBXO21 structure. Analysis revealed that the EID1 peptide's glutamic acid side chains interacted with FBXO21 YccV domain residues lysine (K510, K512) and arginine (R513) within 4Å distance. Through iterative design and docking, we identified carboxylic acid-substituted bi- or terphenyl backbones that mimic EID1 binding to FBXO21. Synthesis and evaluation of substituted bi- and terphenyl analogs identified FBXO21 binders. In vitro ubiquitination assay confirmed that these compounds effectively and selectively blocked FBXO21-mediated ubiquitination, while our designed negative control, did not. Moreover, the novel FBXO21 binders inhibited the growth of AML (HL60 and MOLM13) cell lines with low-nM potencies.

These findings suggest that further development of potent FBXO21 E3 ligase binders into a PROTAC may result in efficient degradation of FBXO21, thereby broadening the therapeutic window for AML treatment. Additionally, this preliminary investigation underscores the discovery of new E3 ligase ligands, representing a significant advancement in the field of targeted protein degradation.

Identifying the molecular determinants of metastatic adaptation in prostate cancer.

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Background: Prostate cancer (PC) is the number one diagnosed cancer in men in the US and the second most common cancer among men worldwide. In turn, PC leads to a significant public health challenge. It was estimated that approximately 288,000 men in the US will be diagnosed with PC in 2023. Understanding metastasis is crucial due to its impact on disease morbidity. The sites of PC metastasis, such as the bone and visceral organs play key roles in disease morbidity. While bone metastasis is common, visceral metastases is associated with poorer survival. The microenvironmental suitability for cancer cells in both bone and visceral organs strengthens their impact on disease progression and treatment outcomes. Further, the exploration of metastatic adaptations involves immune evasion mechanisms, interactions within the tumor microenvironment, and the ability of cancer cells to enter dormancy. Understanding the complexities of PC metastasis, including the molecular mechanisms and adaptation factors, is pivotal for developing effective therapies.

Significance of Problem: Published literature and genetic approaches have uncovered that aggressive metastatic PC display genetic loss of the tumor suppressors PTEN and TP53. To identify the molecular signature of metastatic PTEN/TP53 null cells we performed rigorous multiOmic/ and biochemical analysis of cells derived from tumors at various stages of disease evolution (Pten/Trp53 null mouse model; RapidCaP). This analysis revealed that loss of receptor tyrosine kinase Axl is tightly correlated with metastatic spread to bone and visceral organs. AXL is a member of the **T**yro3**A**xl**M**ertk family of kinases and has shown to be necessary for inducing dormancy like state in PC cells in vivo. Integrating CRISPR-Cas9 technology with robust immunocompetent syngeneic models, our lab has successfully demonstrated that Axl knockout promotes a metastatic phenotype in Pten/Trp53 null cells. However, we lack the mechanistic insight on how of Axl null cells adapt and grow within the metastatic site.

Hypothesis: We hypothesize that the loss of AXL in PTEN/TP53 null cells promotes a metastatic phenotype and plays an essential role in metastatic adaptation. We propose that understanding the biological dependencies of Pten/Trp53/Axl null cells is crucial for therapeutic targeting of metastatic PC.

Experimental Design: To explore this hypothesis we generated a PC metastasis model with Axl knockout (KO; CRISPR) in Pten/Trp53 null RapidCaP derived cell lines. Next, we generated a lung metastasis model (syngeneic) through IV tail vein injection of Axl KO or control Axl WT cells. These *in-vivo* trials enabled the exploration of biological differences between KO and WT cell lines using transcriptomics, immunohistochemistry and multiphoton-photon microscopy-based collagen imaging.

Results/Data: From the current data, we have been able to demonstrate that Pten/Trp53/Axl null PC cells display faster growth, overt lesions and increased metastatic burden when compared to AXL WT cells; based on immunohistochemical presentation within mouse lung tissue. On the contrary the Axl WT cells formed fewer and smaller lesions and prolonged the overall survival of tumor bearing mice. Transcriptomic analysis of Axl KO vs WT cells revealed an enrichment of inflammatory response pathway, increased MTORC1, KRAS signaling and upregulation of protein secretion pathways.

Conclusion: Overall, we have been able to establish a metastatic disease model and began characterizing the biological differences of the model. We have observed that AXL KO cells developed overt metastasis within three weeks whereas the AXL WT cells remain repressed, exhibiting disseminated tumor cells as detected by GFP staining. Further studies need to be conducted to understand the role of the microenvironment and immune systems role in the maintenance of metastatic disease within this model.

REACTIVE ALDEHYDE SPECIES (RASP) INHIBITORS SEQUESTER MAA-ADDUCTS AND REDUCE PRO-INFLAMMATORY CYTOKINES

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Background: Post-translational modifications of self-proteins have been implicated in the pathogenesis of Rheumatoid Arthritis (RA). One of these protein modifications termed malondialdehyde-acetaldehyde-adduct (MAA) has recently gained interest for its involvement in RA. This protein adduct contributes to inflammation by inducing immune cells to generate pro-inflammatory cytokines, T-cell specific responses, responses and circulating autoantibodies. Recently, novel reactive aldehyde species (RASP) inhibitors (ADX-629 and ADX-246) became available that have been shown to prevent the formation of MAA adducts by covalently binding and sequestering MDA and AA in a mouse model of alcoholic liver disease. These inhibitors prevented the release of key inflammatory cytokines and protected animals from progressive liver damage. While these experiments demonstrated the binding of RASP inhibitors to MDA and AA prior to MAA formation, they did not determine the capacity of these agents to scavenge pre-formed MAA protein adducts. Therefore, the purpose of this study was to determine if RASP inhibitors sequester MAA-adducts and block the subsequent cellular release of pro-inflammatory cytokines.

Significance of the problem: MAA modified self-proteins may render harmful effects in patients with RA. Preventing inflammation and inflammation leading to fibrosis by inhibiting cellular binding of could represent significant advancement in the treatment of RA.

Hypothesis: ADX-629 and -246 will prevent MAA protein adducts from binding to macrophage receptors and, as a result, prevent the release of pro-inflammatory cytokines.

Experimental Design: Human monocytic cells (U-937 cell line) were activated to professional macrophages using phorbol 12-myristate 13-acetate (PMA) for 48 hours. Following pre-treatment with decreasing doses of ADX-629 or ADX-246 for 30 minutes, macrophages were incubated with 25µg/mL of fibrinogen (FIB) or MAA-modified fibrinogen (FIB-MAA) for 24 hours. Supernatants were collected for measurement of IL-6 and MCP-1 using commercially available kits. Cells were collected and tested for membrane integrity using a lactate dehydrogenase (LDH) assay.

Results: In the absence of RASP inhibition, FIB-MAA stimulation of cells significantly increased the release IL-6 with mean concentration of approximately 30pg/mL compared to FIB alone 6-fold increase. ($p<0.0001$). IL-6 release was significantly reduced with only 1 µM of ADX-629 and fell to native FIB levels with drug concentrations exceeding 10 µM (**Figure 1A**). ADX-246 demonstrated similar results (**Figure 1B**). Likewise, similar patterns were observed for the release of MCP-1 (data not shown). LDH assays showed no evidence of cellular toxicity regardless of ADX dose.

Conclusions: In addition to confirming the capacity of RASP inhibitors to sequester MAA, results of this study demonstrate that both ADX-629 and ADX-246 attenuate or prevent MAA-modified proteins from initiating the macrophage-mediated release of pro-inflammatory cytokines implicated in RA pathogenesis. These findings support the need for additional *in vivo* investigations of these RASP inhibitors as novel therapies in in the management of RA and possibly in other conditions wherein MAA adducts mediate tissue damage.

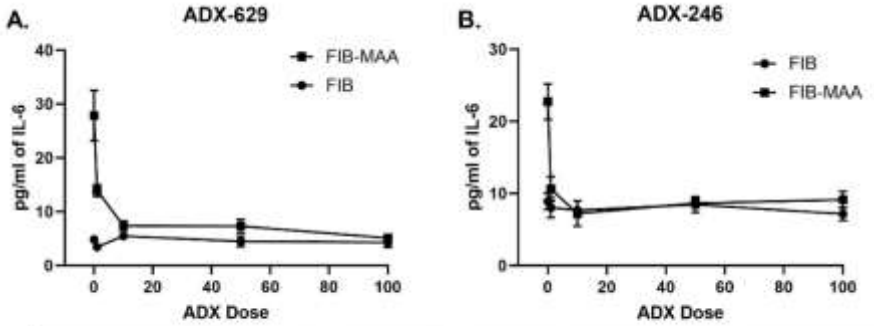

Figure 1. (A) ADX-629 and (B) ADX-246 prevent the release of IL-6 in response to FIB-MAA stimulation. N=5 per group.

TITLE**: RELATIONSHIPS BETWEEN MATERNAL VASCULAR REACTIVITY INDEX AT 24-30 WEEKS GESTATION AND NEONATAL BIRTH OUTCOMES**

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Background: Hypertensive disorders of pregnancy (HDP) affect one in seven pregnancies in the US and can lead to adverse neonatal outcomes, including increased risks of fetal growth restriction, preterm birth, and incidence of cesarean section. Maternal endothelial dysfunction is implicated in the pathogenesis of HDP. Vascular reactivity index (VRI) is a validated, non-invasive measure of endothelial function. Previous studies have shown that VRI is positively associated with well-regarded cardiovascular health indices, including the Framingham risk score and coronary artery calcification score. However, it is unknown whether maternal VRI is associated with neonatal birth outcomes.

Significance of Problem: Endothelial dysfunction is implicated in the pathogenesis of HDP, which can lead to adverse maternal and neonatal outcomes. Currently, a non-invasive and cost-effective method preemptively assessing the risk of HDP development during gestation does not exist. This study aimed to assess the relationship between maternal VRI between 24-30 weeks' gestation and neonatal birth outcomes (e.g. gestational age and birthweight).

Hypothesis: As previous studies have shown that a higher VRI is associated with better cardiovascular health, we hypothesize that maternal VRI will be directly correlated with infant gestational age, birthweight percentile, birth head circumference percentile, and birth length percentile.

Experimental Design: An IRB-approved study enrolled 43 pregnant women at or before 18 weeks' gestation receiving prenatal care at Nebraska Medicine. VRI was measured between 24-30 weeks' gestation using the Endothelix VENDYS machine per manufacturer protocol. In non-pregnant populations, a VRI below 1.4 is considered low reactivity, between 1.4-1.6 is average reactivity and above 1.6 is high reactivity. Birth outcome data was collected from the electronic medical record (EMR). Spearman's R assessed the relationship between continuous neonatal birth outcomes and VRI. A linear regression was performed to adjust for relevant confounders: smoking, maternal age, and hypertensive status. A p-value < 0.05 was considered statistically significant.

Results: Median gestational age at birth was 39.3 weeks, with 50.8% female neonate and 49.2% male. Median maternal age was 32 years old and 42.4% of women had HDP. Median maternal VRI at 24-30 weeks gestation was 1.93 (IQR: 1.69-2.20). Gestational VRI was found to be inversely correlated with birthweight percentile (r_s = -0.437 p=<0.001). After adjustment, a 1 unit increase in VRI predicted a 18.92% decrease in birth weight percentile (95% CI -32.90 to -4.93, p = 0.01). Birth head circumference percentile (r_s = -0.024, p = 0.86), birth length percentile (r_s = -.080, p = 0.05) and gestational age (r_s = -0.227, p = 0.08) were not significantly correlated with maternal VRI.

Conclusion: To our knowledge, our study is the first to assess maternal gestational VRI in relation to neonatal birth outcomes. Counter to our hypothesis, VRI appears to be inversely related to birthweight percentile. Further studies with larger sample sizes are needed to explore this trend, along with stratification of infant sex.

EFFECTS OF THE COVID-19 PANDEMIC ON MATERNAL MENTAL HEALTH

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Background: March of 2020 marked the start of the coronavirus-19 (COVID-19) pandemic, resulting in more than 6.9 million deaths worldwide, a prolonged period of societal lockdowns, and significant job losses due to the spread of severe respiratory syndrome coronavirus 2 (SARS-CoV-2). Though the toll of the pandemic was universal, women experienced more pronounced effects on their mental health than their male counterparts. Pregnancy marks a turbulent period of physiologic change, during which women experience an increased risk of developing psychiatric disorders. Psychiatric conditions that develop during pregnancy put mothers at risk of worsened perinatal outcomes.

Problem: How did the COVID-19 pandemic affect maternal mental health during and after pregnancy?

Significance of Problem: Research suggests that stressors exacerbated by the pandemic such as financial security and health further exacerbated the strain on maternal mental health. However, additional data is needed to fully elucidate the pandemic's impact on maternal mental health during pregnancy.

Experimental Design: A retrospective chart review of 703 mothers was conducted between 2015-2023 with the mothers divided into pre- (06/01/15 to 02/29/20), during- (03/01/20 to 12/31/21), and post- COVID-19 (01/01/22 to 08/31/22) groups based on time of enrollment in a longitudinal observational cohort. Clinical variables such as anxiety, depression, post-partum depression (PPD), history of anxiety or depression, and medication use were collected from the electronic medical record. Descriptive statistics were generated, and Fisher's exact tests associated categorical outcome variables with pre-, during-, and post- COVID timepoints. A p-value of <0.05 was considered statistically significant.

Results: Our study population had 548 (78.0%) pre-, 121 (17.2%) during-, and 34 (4.8%) post- COVID participants. Median maternal age was 29 years. Of this cohort, 458 mothers (71.5%) were white, while 183 mothers (28.5%) were non-white. We observed statistically significant associations between timepoint groups and mental health including anxiety ($p<0.001$), depression ($p=0.006$), PPD ($p=0.013$), medication use ($p<0.001$), and other mental health conditions ($p=0.018$). Percentages of pregnant women experiencing depression, anxiety, and other mental health conditions were highest during COVID and remained elevated post-COVID but returned to pre-COVID levels. Findings are included below:

Variable	Pre-COVID-19 N=548 (78.0%)	During COVID-19 N=121 (17.2%)	Post-COVID-19 N=34 (4.8%)	p-value
Anxiety				
Yes	144 (26.3%)	48 (39.7%)	18 (52.9%)	<0.001
No	404 (73.7%)	73 (60.3%)	16 (47.1%)	
Depression				
Yes	150 (27.4%)	50 (41.3%)	13 (38.2%)	0.006
No	398 (72.6%)	71 (58.7%)	21 (61.8%)	
Post-Partum Depression				
Yes	62 (11.3%)	26 (21.5%)	5 (14.7%)	0.013
No	486 (88.7%)	95 (78.5%)	29 (85.3%)	
Medication Use for Mental Health				
Yes	66 (12.0%)	35 (28.9%)	8 (23.5%)	<0.001
No	482 (88.0%)	86 (71.1%)	26 (76.5%)	
Other Mental Health Conditions				
Yes	223 (40.7%)	65 (53.7%)	18 (52.9%)	0.018
No	325 (59.3%)	56 (46.3%)	16 (47.1%)	

Conclusions: This study supports other work elucidating the COVID-19 pandemic's impact on worsening mental health among pregnant women. Future directions include determining pandemic stressors that exacerbated mental health the most as well as determining support programs and resources that support the mental health of pregnant women.