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2015 FACE RESEARCH NETWORK POSTER COMPETITION ABSTRACTS

1.

A meta-analysis comparing executive functioning in children and adolescents prenatally exposed to alcohol compared to controls and individuals with attention deficit/hyperactivity disorder

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Source of Funding: None
Conflict of Interest: None

Background/ Objectives: Extant research consistently identifies executive functions (EF) as a central impairment associated with Fetal Alcohol Spectrum Disorders (FASD). Despite this, heterogeneity exists regarding the strength of the association between FASD and EF, and findings have not yet been quantitatively synthesized. Further, it remains unclear whether EF deficits differ between FASD and other clinical populations.
Methods: This meta-analysis included 46 studies examining the relation between FASD and EF. All studies compared children and adolescents with a diagnosis of FASD to healthy control participants. A subset of 13 studies compared FASD to ADHD participants. Following Miyake Emerson, Witzki, and Howerter's (2000) model of EF, working memory, inhibition, and set shifting were the EF examined.
Results: When compared to healthy controls, children with FASD demonstrated significant deficits across these EF (d = 0.67 [0.56, 0.77]). Magnitude of the effect differed by type of EF, with working memory (d = 0.67 [0.50, 0.85]) and inhibition (d = 0.65 [0.50, 0.80]) yielding medium effects and set shifting yielding a large effect (d = 0.84 [0.70, 0.99]). Several characteristics of the sample, nature of prenatal exposure, and EF methodology significantly moderated these results. A secondary meta-analysis of studies examining FASD and ADHD suggested that the relation between weaknesses in EF and FASD is stronger than that found for children with ADHD only (d = 0.25 [0.17, 0.34]). Interestingly, only IQ emerged as a significant moderator, such that FASD samples with lower IQ had greater EF deficits compared to ADHD samples.
Conclusions / Discussion: These findings support the notion that FASD is broadly related with EF deficits, though important nuances exist within these associations. These deficits are greater than those with ADHD, particularly for children who present with low IQ. Research and clinical implications will be discussed with regards to the neurodevelopmental considerations within FASD populations.
Key Words: *Executive functioning, FASD, meta-analysis*

2.

Developmental pathways to alcohol use and binge drinking among Inuit pregnant women

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Source of Funding: The National Institute of Environmental Health and Sciences/NIH (R01-ES07902), Indian and Northern Affairs Canada (Northern Contaminants Program), Health Canada, Hydro-Quebec (Environmental Child Health Initiative), the Public Health Direction for the Nunavik Regional Board of Health and Social Services, the Joseph

Young, Sr., Fund from the State of Michigan, the Canadian Institutes of Health Research, and the Nasivvik Centre for Inuit and Changing Environment.
Conflict of Interest: All authors have been personally and actively involved in substantive work leading to the report and all relevant ethical safeguards have been met.

Background: While annual frequency of alcohol consumption in the Inuit population is relatively low and abstinence is high,[1,2] amount of alcohol consumed per drinking day is high and the episodes of binge drinking are three times more frequent than in the Canadian population, independently of gender.[1,3] Developmental pathways of drinking pattern among Inuit pregnant women are of particular interest while the alcohol use of women during pregnancy may lead to harmful effects on the fetus.[4-6]
Objective: Investigate developmental pathways to alcohol use and binge drinking among Inuit women from the period preceding the pregnancy to the end of the post-partum year, and establish whether specific factors could be identified as predictors of changes in alcohol behaviors.
Methods: Markov modeling was used to describe the movement among alcohol users (i.e. non-drinking and drinking) and binge drinkers (i.e. non-binging and binging) across 4 time periods (before the pregnancy, at conception, and during and after the pregnancy). 248 women from Nunavik (Quebec, Canada) were inquired on 3 distinct occasions to provide descriptive data on their alcohol use (Nunavik Child Development Study, 1996-2011).
Results: Both alcohol use and binge drinking developmental pathways demonstrated a significant drop around the conception period but rise back during the pregnancy. We also noted high probabilities of becoming an abstainer or not binging at this time. Women in couple and not using marijuana were more likely to stop binge drinking at conception.
Conclusions: This study emphasized the importance of the conception period in the definition of the drinking pattern around pregnancy. The importance to consider alcohol use and binge drinking in a multidimensional way (personal, familial and social determinant) is also addressed while trying to limit harmful effects of alcohol consumption both to women and their fetus.
Key Words: *Pregnancy, Inuit, Markov models*

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3.

What do Ontario health care professionals know about Fetal Alcohol Spectrum Disorder? A secondary data analysis of the FAS survey for health professionals

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Source of Funding: Ontario Graduate Scholarship (OGS)
Conflict of Interest: None

Background: Health care professionals play a central role in the prevention of FASD, particularly through guidance regarding alcohol use during pregnancy. Given that women rely heavily on the *expertise* received by their providers (Anderson, Hure, Kay-Lambkin, & Loxton, 2014), it is vital to have professionals who are educated about FASD. National survey results suggest that Canadian health care professionals, while aware of some aspects of FASD, require further training and education (Clarke, Tough, Hicks, & Clarren, 2005). However, the level of knowledge of FASD held by Ontario professionals has not been investigated.
Methods: A secondary data analysis was conducted using data obtained from the 2001-2002 Fetal Alcohol Syndrome (FAS) Survey for Health Professionals. Ontario-specific data (n=884) was used to examine the knowledge, attitudes, and awareness of FASD held by various health care professionals (e.g., family physicians, paediatricians, psychiatrists, midwives, family physicians, obstetricians).

Results: Preliminary descriptive data has been conducted at this time. Nearly all (99.5%) of the surveyed professionals in Ontario had previously heard of FAS. The majority (92.1%) of these professionals either agreed or strongly agreed that prenatal alcohol exposure poses a significant risk factor for brain damage. However, only 72.3% reported discussing the risks of alcohol during pregnancy and only 87.9% of respondents recommended that pregnant women completely abstain from alcohol for the duration of their pregnancy. Furthermore, only 62.4% agreed with the practice of telling patients to drink 'in moderation'. Significant differences were noted between medical specialties in their definition of "moderation". On average, family physicians considered a greater number of drinking occasions per week to be moderate (M=3.44, SD=2.32) compared to paediatricians (M=2.31, SD=1.90) and midwives (M=2.51, SD=2.36) ($F_{(4,788)}$=4.41, p=0.002). Further data regarding differences between medical specialties and rural/urban practice location will be available for this poster.

Conclusion/Discussion: Although this data is somewhat dated, the results of this secondary data analysis are relevant as they support findings that consistent recommendations are not provided by health care professionals when advising women of childbearing age about alcohol use. The results provide a starting point for better understanding the knowledge and awareness of professionals in Ontario.

Key Words: *Fetal Alcohol Spectrum Disorder, secondary data analysis, health care professionals, rural health, knowledge*

4.

Epigenetic footprints in FASD etiology, insights from human and mouse models

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Source of Funding: NSERC

Conflict of Interest: The authors declare no conflict of interest.

Background: Epigenetic marks, such as the modification of DNA (DNA methylation) or the proteins that package it (histone modification) govern normal development. Epigenetic marks are sensitive to environmental influence and are associated with many human diseases. Our group has focused on DNA methylation changes in a mouse model of FASD. We are also studying DNA methylation in cheek swabs from children with FASD. We hypothesize that ethanol-induced DNA methylation changes in cheek swabs and mouse hippocampus are similar. Furthermore, that DNA methylation can serve as an effective proxy to infer epigenetic changes in response to neurodevelopmental alcohol.

Methods: Cheek-swab DNA was collected from children ages 3-10 diagnosed with FASD and matched controls from Midwestern Ontario. DNA and chromatin were extracted from hippocampal tissue of young-adult (70 day old) mice. DNA was used for DNA methylation microarray analysis and chromatin for chromatin immunoprecipitation microarray.

Results: Both human and mouse studies indicate that fetal ethanol exposure leads to genome-wide changes in DNA methylation. Changes occur at many genes, and overlap between mouse and human. The protocadherin genes, which govern synaptic development, were significantly affected in both. We also found disruption of histone modifications at protocadherin genes in mice.

Conclusion/Discussion: The DNA methylation results presented here may serve as novel biomarkers for early diagnosis of FASD. Changes in such genes and pathways also may be the target of future epigenetic therapies for FASD symptoms.

2015 FACE RESEARCH NETWORK PODIUM PRESENTATION ABSTRACTS

1.

Unique and interactive effects of prenatal alcohol exposure and early-life adversity: focus on mental health

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Source of Funding: Canadian Foundation on Fetal Alcohol Research (CFFAR) grant to CR and JW, and NIH/NIAAA grants R37 AA007789 and R01 AA022460, and NeuroDevNet grant 20R64153 to JW.
Conflict of Interest: The authors declare no conflict of interest.

Background/Objectives: Despite remarkable progress identifying and characterizing effects of prenatal alcohol exposure (PAE), relatively few studies have investigated how the early-life environment contributes to pervasive, long-lasting effects of PAE. Importantly, children prenatally exposed to alcohol are, in general, more likely to encounter stressful and/or abusive environments during infancy. Combining two rodent models, we examine the unique and interactive effects of PAE and early-life adversity on the offspring.
Methods: Pregnant rats were assigned to either PAE – liquid ethanol diet *ad libitum*; Pair-fed (PF) – liquid control diet yoked to PAE consumption; or Control – pelleted control diet *ad libitum*. To model early-life adversity, half of these mothers were exposed to a limited bedding environment from postnatal day (P) 8-12, during which we recorded maternal behavior and pup vocalizations. Male and female offspring were tested in tasks assessing anxiety- (open field [OF] and elevated plus maze [EPM]) and depressive-like (forced swim test - FST) behaviors and working memory (object recognition). As the immune system can also play a role in mental health, we also evaluated challenge-evoked immune system responses.
Results: Insufficient bedding induced abusive-like maternal behavior across all groups. However, PAE pups vocalized less in response to early-life adversity. Our preliminary analyses of the OF indicate that PAE increased anxiety-like behaviors in females and early-life adversity increased anxiety-like behaviors in control females. Similar to the OF, we observed differential effects of PAE and early-life adversity in the EPM, FST and object recognition tests. Additionally, following early-life adversity, PAE males fail to show normal recruitment of immune cells in response to an immune challenge.
Conclusions/Discussion: Our results indicate that despite similar abuse-like maternal behaviors across prenatal groups, PAE pups vocalize less in response to early-life adversity. Moreover, results from later-life emotional, cognitive and immune responses demonstrate unique and interactive effects of PAE and early-life adversity.
Key Words: *Prenatal alcohol exposure, early-life adversity, psychopathology*

2.

Effect of postnatal environment on learning and memory in FASD

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Source of Funding: Western Graduate Research Scholarship, Canadian Institutes of Health Research, Natural Sciences and Engineering Research Council of Canada
Conflict of Interest: There is no conflict of interest on behalf of all authors

Background/Objectives: Maternal drinking causes FASD characterized by cognitive abnormalities including learning and memory deficits. The severity of these abnormalities is often attributed to the dose and timing of exposure as well as the postnatal environment. In this research we have assessed the importance of negative and positive postnatal environments on the manifestation of learning deficits in an animal model using C57BL/6 mice.
Methods: Experimentally, we have established that prenatal alcohol exposure causes learning deficits in our mouse model. Alcohol-exposed mice and matched controls were subjected to two different postnatal environments: early-life stress to simulate a neglectful

environment detrimental to the developing child and positive environmental enrichment consisting of physical exercise and cognitive stimulation, to resemble specialized classrooms, activities and counseling sessions. We evaluated behavioural and cognitive performances and collected genetic material from brain samples.
Results: FASD-like mice, relative to control mice exhibit high anxiety-like traits with decreased memory performance. Importantly, early-life stress exacerbates these behavioural outcomes. Environmental enrichment ameliorates these deficits to a certain degree. We are currently working on investigating molecular mechanisms behind these behavioural outcomes.
Conclusions: The postnatal environment has a significant effect on modulating the spectrum of behavioural and cognitive deficits that arise due to prenatal alcohol exposure. Our results replicate similar observations made in human FASD cases. Early-life stress worsens behavioural and learning deficits characteristic of FASD. With a positive and nurturing environment, it is possible to ameliorate some, if not all of these deficits. These findings are translatable to human FASD cases, where a nurturing and positive environment can help improve behavioural outcomes. Our results may be helpful in suggesting moderation/treatment strategies that can be used by nurses, counselors and policy-makers.
Key Words: *Learning, brain, postnatal environment*

3.
MRI of brain development in FASD

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Funding: Canadian Institutes of Health Research (CIHR) and NeuroDevNet
Conflicts of Interest: None

Background: Despite obvious behavioural and cognitive impairments, brain abnormalities associated with FASD are not typically 'visible' with routine clinical brain imaging. The goal of this work is to use advanced quantitative magnetic resonance imaging (MRI) methods that have the capacity to uncover more subtle deviations in brain development associated with FASD.
Methods: MRI scans and cognitive assessments were obtained in both cross-sectional (n=149 FASD, n=152 controls, 5-32 years old) and longitudinal (n=17 FASD, n=21 controls, 5-15 years old) cohorts. White matter microstructure, brain volumes and cortical thickness were compared between groups, as well as their changes with age and links to cognitive scores and head circumference.
Results: Cross sectional analysis showed that the FASD group had poorer white matter microstructure, reduced cortical thickness, and smaller brain volumes, the latter being the most robust difference relative to controls. Brain volume and head circumference correlated for most FASD subjects; however, the correlation was not significant in those with head circumferences well below the population norm. Longitudinal analysis revealed altered developmental trajectories of white matter and cortical thickness in children and adolescents with FASD, but no differences in the rate of brain volume change with age. Notably, FASD subjects with greater changes in reading score over several years had correspondingly larger changes in white matter microstructure in two white matter tracts previously implicated in language function.
Discussion: Together these studies confirm regional abnormalities in brain structure and deviations in brain development with age that may reflect differential vulnerability to injury from alcohol in utero. However, no metrics had sufficient separation from controls to be diagnostic in FASD. Nonetheless, these findings have expanded our understanding of central nervous system impairments associated with prenatal alcohol exposure, and have confirmed that the combination of multiple features may be required to establish an imaging biomarker for FASD.
Key Words: *MRI, brain structure, FASD*

4.
A prospective follow-up study of adolescents with Fetal Alcohol Spectrum Disorder: risk factors for the development of conduct problems

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Source of Funding: The Canadian Institute of Health Research and Glendon College.
Conflict of Interest: The presenting author and all other co-authors have no conflict of interest to declare.

Background/Objectives: Prenatal alcohol exposure (PAE) has consistently been linked to later conduct problems (CP). This study aims to further elucidate how multiple bio-psychosocial risk factors, often co-occurring with PAE, function together to predict CP in adolescents with fetal alcohol spectrum disorder (FASD).
Methods: This study was part of a larger prospective follow-up study of adolescents diagnosed with FASD at The Hospital for Sick Children (N = 63). Data for the following predictors, selected in light of the biopsychosocial model of CP, were collected during initial diagnostic assessments: sex, age, maternal criminality, abuse history, number of caregiver placements, behavioural/emotional regulation skills (measured by the Behaviour Rating Inventory of Executive Function), and social problems (measured by the Conners' Parent Rating Scales – Revised). Outcome variables, collected two to seven years post-diagnosis, included caregiver-rated aggressive and rule-breaking behaviour on the Child Behaviour Checklist (CBCL), self-reported delinquency/criminality on the Global Appraisal of Individual Needs – Short Screener (GAIN-SS), and adolescents' legal history. Separate multiple linear or logistic regression models were constructed to examine the simultaneous effects of the selected predictors on each outcome variable.
Results: Poor behavioural/emotional regulation was the only significant unique predictor of CBCL Aggressive Behaviour *T*-scores (B = 0.29, p = .040) and of GAIN-SS Crime/Violence Screener scores (B = 0.07, p = .037). The multiple linear regression models including the selected biopsychosocial predictors explained a significant proportion of variance in adolescents' Aggressive Behaviour (R^2 = 0.24, $F(7, 51)$ = 2.26, p = .044) and Crime/Violence Screener scores at follow-up (R^2 = 0.25, $F(7, 50)$ = 2.42, p = .033). Conversely, there were no significant predictors of CBCL Rule-Breaking Behaviour *T*-scores. Finally, sex (OR = 11.90) and the number of caregiver placements (OR = 1.72) significantly increased the odds of having committed a criminal offence.
Conclusions/Discussion: Results show that self-regulatory skills are particularly critical to the development of CP in youth with FASD. Intervention efforts aimed at preventing CP in individuals with FASD should focus on improving self-regulation skills and promoting a stable and nurturing home environment.
Key Words: *Fetal Alcohol Spectrum Disorder, prospective follow-up, conduct problems*

5.
Reducing the prevalence of FASD primary and secondary disabilities using a community based approach to FASD prevention in an Atlantic First Nation

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Source of Funding: None
Conflict of Interest: None

Background/Objectives: While we do know that FASD affects people of all races and ethnicity there is evidence FASD prevalence rates in some aboriginal communities are as high as 20%. This data is not generalizable but it does indicate a serious gap in terms of health status in aboriginal communities. This presentation will explore prevalence rates in a Canadian aboriginal community at two points in time. It will discuss the development of community and culturally based programs and approaches implemented by the community after high FASD prevalence was established. Was the community approach effective? Are FASD prevalence rates lower in 2014-2015 than they were in 1999-2000?
Methods: Research design—School-based FASD prevalence study.
Study population—School age children attending a FN Band operated elementary school screened for PAE and assessed for FASD at two points in time- 15 years apart. The first group was followed longitudinally for 15 years after diagnosis and were screened for select secondary disabilities including: trouble with school, trouble with law, trouble with addictions.
Setting: Indigenous community
Procedures for data collection and the analysis (including statistical techniques)—SPSS, Descriptive statistics. *Review the findings from the original FASD school prevalence study.* In 1999-2000 a needs assessment was undertaken in a FN community school. Approximately 20 % of the children in the school population were subsequently diagnosed with an FASD.
Review the diagnostic, prevention and intervention services and tools developed
Over the last decade an FASD service delivery model was developed in the community that included development of culturally based screening and diagnostic tools, access to community based diagnostic team, implementation of school interventions and an

FASD mentoring and outreach program for pregnant and high risk women.
Establish the present prevalence of FASD's in the community school
For conceptual, institutional, educational, or policy papers:
This community based model of FASD prevention is a 4 level prevention model developed with the input of community elders, parents and service providers during a series of community focus groups and meetings. It is similar to Leavell and Clark's 1965 3 level prevention model rather than the present PHAC model of FASD prevention
Results: In 1999-2000 there was FAS prevalence in the community school of over 5%. In 2014-15 there was 0% FAS in the community school. There was no FAS diagnosis since 2005. Rates of other FASD's have also been significantly lowered. There are also fewer siblings affected by FASD, Overall FASD prevalence rates have dropped from approximately 20% - 12.5%. Economically this means lifetime savings of millions of dollars for both the community and province.
Conclusion/Discussion: Through an expanded community based model of prevention both the prevalence of FASD and severity of secondary disabilities associated with FASD can be shown to have been lowered. Despite these findings the prevalence rate of other FASDs continues to be higher than in the general population. FASD rates in the community are 12.5% compared to 1-5% in the general population. Women continue to smoke cigarettes during pregnancy and there are much higher rates of pre-natal exposure to other drugs. Research indicates community based interventions have been effective but more outreach programs are needed at all levels and for at-risk sub-populations in the community system.
Key Words: *FASD prevalence, FASD prevention, school-based prevalence study*

6.
Alcohol use among Inuit pregnant women: how valid are drinking measures over time?

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Source of Funding: The National Institute of Environmental Health and Sciences/NIH (R01-ES07902), Indian and Northern Affairs Canada (Northern Contaminants Program), Health Canada, Hydro-Québec (Environmental Child Health Initiative), the Public Health Direction for the Nunavik Regional Board of Health and Social Services, the Joseph Young, Sr., Fund from the State of Michigan, the Canadian Institutes of Health Research (RN188397-299895), and the Nasivvik Centre for Inuit and Changing Environment.
Conflict of Interest: **All authors been personally and actively involved in substantive work leading to the report and all relevant ethical safeguards have been met.*

Background: Several indicators have been used to estimate the risks of women's alcohol consumption during pregnancy on the development of the future child, such as frequency, quantity and measure of intoxication (binge drinking).[1-4] Moreover, women's alcohol consumption may be evaluated during the pregnancy (prospective studies) or after the pregnancy (retrospective studies). Some studies already compare the validity of alcohol report during pregnancy between prospective and retrospective studies.[5-6] However, such data were not available for the Inuit population.
Objective: Evaluate the agreement between indicators of alcohol use and binge drinking during pregnancy and 11 years after the delivery among Inuit women from Nunavik (Northern Quebec, Canada).
Methods: The study sample includes 67 women who were enrolled in the Nunavik Child Development Study while pregnant (between 1995-2000) and followed when their child reached 11-year of age. Women were interviewed with regard to their alcohol consumption during pregnancy (use -yes/no-; binge drinking -yes/no-) while they were pregnant and 11-year after delivery. Over time agreements on alcohol use indicators were estimated using Kappa of Cohen (SPSS 20.0).
Results: During pregnancy, 65.7% of women reported to consume alcohol and 40.3% to binge drink. Eleven years later, fewer participants reported to have drunk alcohol during pregnancy (31.3%, $p < 0.001$) and to have binge drink (22.5%, $p < 0.002$). A fair agreement ($k = 0.28$, $p < 0.004$) on status of alcohol user (yes/no) during pregnancy was obtained between the prenatal and the 11-year assessment, while a moderate agreement ($k = 0.47$, $p < 0.001$) was obtained for binge drinking status.
Conclusions: In contrast to studies conducted among

non-aboriginal populations, our study conducted with Inuit women depict a fair to moderate agreement of alcohol indicators when interviews are conducted during pregnancy or years after delivery. Our results support during rather than after pregnancy report**.**

Key Words: *Pregnancy, Inuit, over time agreement*

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7.

Stigma and FASD: accounting for the ethical implications of stigma in public health practices

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Source of Funding: NeuroDevNet
Conflict of Interest: The authors have no conflict of interest to disclose.

Background: Stigma can influence the prevention and identification of fetal alcohol spectrum disorder (FASD), a leading cause of developmental delay in North America. While some aspects of the stigma experienced by pregnant women using alcohol or drugs have been discussed, including their experiences of fear, shame and blame, there is little literature that has examined the experience of negative judgments across the life course for individuals with FASD and their families. There are also significant gaps in our understanding of the impact of public health practices or policies, and the ways that these may inadvertently increase the stigma felt or experienced by those affected by FASD. These gaps raise important ethical questions about the intents and outcomes of public health practices or policies.

Methods: We conducted a review of social and biomedical literatures about stigma and mental health, neurodevelopmental disorders, and disability; we reviewed qualitative research about the experiences of individuals with FASD, and identified relevant and related literatures from these original sources. Using a broad review strategy we hoped to gain further insight into the pervasiveness of stigma and highlight common traits of felt or enacted stigma on individuals and families affected by developmental conditions.

Results: Three themes around stigma were drawn out from our literature review: (i) personal responsibility and blame towards biological mothers; (ii) felt and enacted stigma experienced by children and families; (iii) anticipated life trajectories for individuals with FASD.

Discussion: The ethical implications of stigma rest on two distinct criteria (dignity and consequences); public health practices must resolve to avoid negative impacts of stigma on the person or family. We recommend further empirical and ethical analyses to examine whether public health policies and practices inadvertently stigmatize those affected by FASD.

Key Words: *Ethical analysis, stigma, public health*