Acne, Depression, and Anxiety Symptoms in Young Adults

Janice Hammill

Thesis submitted to the University of Ottawa

in partial Fulfillment of the requirements for the

Master of Arts in Education, Counselling Psychology

Faculty of Education

University of Ottawa

Table of Contents

Acknowledgements

I am sincerely grateful for the incredible mentorship and guidance I have received from such a remarkable team of women throughout the pursuit of my Master's degree. Thank you, Dr. Tracy Vaillancourt, for your years of dedication to building a team of intelligent and powerful role models that I am fortunate enough to learn from, work with, and admire. I could not have completed this academic milestone without your invaluable feedback, patience, humour, and insight. Your contagious determination has taught me to achieve what I am capable of. The vision you held for what I could accomplish has set a new precedent for my vocational and academic goals. The ceaseless devotion you show to high quality research, and the mental health, safety, and education of youth across Canada, and the world, is formidable. I am so thankful to have studied under your lead.

Thank you to the Brain and Behaviour lab members for your amazingly supportive and constructive comments on each and every draft of this paper you reviewed, and for sharing your beautiful, curious, and intelligent minds with me over the last few years. Every one of you have contributed to my success and development as a young researcher and clinician. Heather, your time and commitment to my academic journey cannot go unmentioned and I am deeply thankful to have had access to your mind and statistical super powers. Dr. Krygsman, your knowledge, patience, and continual kindness are truly amazing and I cannot thank you enough for the time and energy you put towards helping me reach this goal. I would also like to thank the members of my thesis committee, Dr. Diana Koszycki and Dr. Anne Theriault for their time and expertise in their evaluation of my work.

Finally, thank you to my closest friends and colleagues who supported me during this process with their laughter, critical feedback, impressive clinical and academic insight, and most importantly, by not letting me procrastinate half as much as I would have. The relationships and memories I have made throughout this experience are a lasting reminder of how far we've come and I am so excited to continue to work with all of you. Thank you to my family and friends for the unmatched support in pursuing this degree. I could not have achieved this without your love, resources, and bottomless encouragement. And, to all those I have met and learned from throughout this winding academic road, thank you. We did it.

Academic Contributions

Charlotte Hammill was the first author of the paper entitled "Acne and Its Association with Internalizing Problems". The first author contributions included the comprehensive literature review, writing of the manuscript, and incorporation of suggestions made by Dr. Vaillancourt. Dr. Vaillancourt was the second author of this paper and provided feedback and recommendations regarding the structure and content of the review. Dr. Vaillancourt is the first author's thesis supervisor.

Charlotte Hammill was the first author of the paper entitled "Acne, Major Depression, and General Anxiety in Young Canadian Adults". The first author responsibilities included the literature review, statistical planning and analyses, and incorporation of edits from co-authors. Charlotte also contributed to data collection, entry, and cleaning at Time 12, 13, and 14 (i.e., 2020-2022) of the McMaster Teen Study. She was actively involved in participant recruitment and follow up, and survey design and implementation. Dr. Vaillancourt was the senior author and is the primary investigator of the McMaster Teen Study. She is also the thesis supervisor to the first author. She supported the planning and implementation of the statistical design and provided feedback regarding paper content and structure. Dr. Amanda Krygsman was the second author of this study; she contributed to statistical planning and analysis of the results and verified all statistical processes. Heather Brittain was the third author of this study and provided guidance and feedback regarding statistical planning and analysis. Dr. Krygsman and Ms. Brittian are the study coordinators of the McMaster Teen Study and have participated in data collection, design, and analysis since its inception.

Abstract

Elevated risk and prevalence of internalizing symptoms and diagnoses such as Major Depression (MDD) and Generalized Anxiety Disorder (GAD) are documented in patients with acne, but longitudinal studies remain scarce. Moreover, little is known about the moderating role of gender in this relation and few studies have assessed Canadian samples. Evidence also shows that hormonal contraceptives may mitigate internalizing symptoms for women and is a common treatment for acne. This thesis is comprised of two parts: (1) an extensive narrative review that was published in April 2023 in *Dermatological Reviews* and (2) an empirical longitudinal study. The narrative review highlighted the theoretical foundation and cross-sectional evidence that implicates acne as cross-cultural risk factor for depression, general anxiety, and social anxiety symptoms. The review also considered the role of hormonal contraceptives in this relation for women. The empirical study examined the longitudinal relation between acne, depression, and anxiety symptoms concurrently and across 3 annual time-points in a sample of Canadian young adults aged 21-23 years old. Self-reported severe acne predicted elevated anxiety symptoms at age 22 when controlling for concurrent depression and gender. Self-reported severe acne at age 22 predicted elevated anxiety at age 23 when controlling for prior depression and anxiety symptoms for men only. There was no association between internalizing symptoms and acne for women and hormonal contraceptives did not alter this finding. Our study showed longitudinal support for previous cross-sectional evidence that implicates acne as a risk factor for anxiety symptoms. Men may be more negatively impacted than women over time. Physicians should carefully attend to emerging adult-males with severe acne by screening for anxiety and provide rapid acne treatment to reduce their mental health burden.

Part 1: Acne and its Association with Internalizing Problems

Introduction

The skin is the body's largest[1] and most visible organ that communicates meaningful, biological and social information (e.g., facial expressions, attractiveness, ethnicity, health) [2, 3] central to our identities. Past research has shown that people living with skin conditions that alter or disfigure the appearance of skin such as acne vulgaris, dermatitis, psoriasis, or vitiligo carry a considerable burden of disease[4] and often endure poor mental health (e.g., depression, anxiety, suicidality, poor body image) [5, 6] social, emotional, and vocational challenges (e.g., romantic, sexual, and employment difficulties)[7, 8] and diminished quality of life [9]. Of such conditions, acne vulgaris, hereafter referred to as "acne", is a skin disorder involving clogged pilosebaceous units that can present as inflammatory (i.e., pustules and papules or "whiteheads") or non-inflammatory (i.e., open comedone or "blackhead") facial or body lesions.[10, 11] Acne is the most common dermatological complaint seen by physicians and affects approximately 9.4 % of the global population.[12-14] Though acne is widely prevalent, 80-85% of its sufferers are between the ages of 12 and 25,[13] making this often-upsetting condition, and its problematic psychosocial side effects, a defining feature of adolescence and young adulthood. Concerningly, acne takes a significant psychosocial toll on its sufferers by impacting physical appearance.[15, 16] Indeed, previous studies have illustrated a worrisome picture for those with acne and indicate elevated risk for sub-clinical risk factors (e.g., low self-esteem, social avoidance)[17, 18] and clinical diagnoses of depression,[6] suicidality,[19, 20] social,[23] and generalized anxiety disorder, compared to those without acne.[19-25]

Teens with acne have reported lower attachment to friends,[20] poor self-esteem,[22] decreased dedication to school,[23] reduced intention to participate in extracurricular activities,[23] and anger.[24, 25] Likewise, studies of adults report problematic subclinical indicators such as feelings of immaturity,[26] self-consciousness,[27] and insecurity because acne is typically viewed as a "teenage problem".[28, 29] These difficult emotions have been shown to impede critical life facets such as employment security,[8] romantic relations, and sexual satisfaction,[7] extending the negative impact of acne far beyond just that of physical appearance.

Some researchers have noted that adolescents may be vulnerable to psychosocial morbidity because acne typically arrives during puberty,[30-32] a period of substantial physical, social, and psychological change. During puberty, hormones such as androgens increase in

production which can increase the size of the body's oil glands and oil production to result in clogged pores or acne.[10, 33] Throughout this period of remarkable change, acne can act as an additional stressor to an already perplexing stage of development that is characterized by a heightened concern with physical appearance,[34] emphasis on peer acceptance,[34, 35] sensitivity to social evaluation, and emerging self-image.[36] As adolescents mature into young adults, acne may exacerbate core symptoms (e.g., a negative self-view, excessive worrying, fear of social evaluation) of internalizing disorders such as major depressive, general, and social anxiety disorder, that surge in incidence during this developmental period (i.e., 18-29 years of age).[37, 38] Acne can also be judged as a developmental rarity in young and middle adulthood, leading to heightened feelings of stigmatization for this age group. [28, 39] In addition, persistent acne that carries into adulthood may be accompanied by negative psychosocial consequences related to prolonged battles with effortful and expensive remedies. [27, 28, 40, 41]

Consequently, cumulative research demonstrates that acne is distressing for a broad range of ages and cultures.[42] The most recent meta-analysis of 42 cross-sectional studies conducted by Samuels et al. (2020), showed that clinical depression was more prevalent in youth (i.e., 12-19 years old) and adults (+19 years) with acne compared to their non-acne counterparts (r = .22, p <. 00001). [42] This finding was true for both community and clinical samples, with the strongest association between acne and depression appearing in the clinical adult sample, though the authors cautioned against overrepresentation of adults in the clinical acne samples. [42] The results were similar for anxiety such that it was more prevalent in youth and adults with acne (r = .25, p < .00001), though significant associations were only found in the clinical acne samples (r = .32, p < .00001) and not the community samples (r = .08, p > .05).[42] In general, adults reported higher rates of depression and anxiety than youth, which aligns with the societal and developmental norms described above whereby acne is commonly viewed as a teen issue. [42] This review included studies from the UK, the Middle East, Central, South and East Asia, New Zealand, and Nigeria indicating that the mental health burden associated with acne is a global concern. [42] Notably, there was only one North American study conducted in the U.S. in this review and no Canadian studies. [42] Although little is known about the impact of acne on mental health in young Canadians, acne likely thwarts psychosocial adjustment of its sufferers irrespective of culture.[22, 42]

In 2019, depressive and anxiety disorders affected approximately 3.75% and 4% of the global population, respectively, and continue to carry one of the largest burdens of disease.[43, 44] Of note, some researchers have reported increased prevalence rates for both depression and anxiety as the COVID-19 pandemic has persisted (e.g., Racine et al., 2021; Santomauro et al., 2021)[45, 46], though the literature awaits longitudinal studies to corroborate this trend. Nonetheless, identifying people at risk for depression and anxiety is a top priority given their onerous impact on the social and emotional well-being.[47, 48] Major depressive disorder (MDD) is the most common mood disorder and is characterized by persistent low mood, altered sleep and eating patterns, low enjoyment in pleasurable activities, and social withdrawal.[37] In younger populations, the DSM-5 criteria of low mood can be replaced with persistent irritability.[37]Age of onset for major depression can vary, though young adults aged 18-29 years-old often exhibit the highest prevalence [37] with disorder reoccurrence linked to greater impairment.[49, 50] For young adults, MDD can derail academic and vocational success,[51] impede socialization and friendships, [52] and is a primary risk factor for suicide,[53] which is a top cause of death in this age group.[54] MDD is often comorbid with generalized anxiety disorder (GAD),[55] which is characterized by excessive, recurrent, and uncontrollable worry for a period of at least six months and is accompanied by physical symptoms such as feeling on edge, muscle tension, or fatigue.[37] Like MDD, diagnosis of GAD is associated with an onslaught of future difficulties including disorder reoccurrence, higher risk for comorbidities like substance use,[48] poor physical health,[56] and unemployment in adulthood.[57] Social anxiety disorder (SAD) is also commonly comorbid with MDD and GAD[37, 58] and shares unique and similar debilitating outcomes (e.g., social isolation[58] and substance use [48]). SAD is characterized by marked fear of evaluation and scrutiny by others, and excessive fear of social embarrassment. [37, 58] Feared social situations are avoided altogether or are endured with strong discomfort.[37] Most previous studies that have examined acne and internalizing disorders have used measures of MDD, GAD, and SAD symptoms or diagnoses [42, 59] and thus, are reviewed here.

In a recent review, Natsuaki and Yates (2021) emphasized that acne and its relation to poor mental health has remained in the peripheral of the dermatological and developmental psychology literature, despite descriptive studies (e.g., qualitative, cross-sectional, archival) and meta-analytic findings that demonstrate negative effects on psychosocial well-being for multiple age groups and cultures.[60] To extend the work of Natsuaki and Yates (2021), the aim of this

narrative review is to further synthesize the literature regarding acne and its relation to mental health with a specific focus on internalizing symptoms and diagnoses of MDD, GAD, and SAD.[60] The manifestation of internalizing symptoms is explored using a sociocultural framework that identifies exposure to and internalisation of beauty ideals and appearance-based psychosocial judgements as critical stakeholders in the relation between acne and mental health. Our narrative review also considers the role of hormonal contraceptives and isotretinoin (e.g., Accutane), primary treatments for acne that have been linked with internalizing symptoms.[61-63]

Acne Prevalence and Course

Generally, acne first appears during puberty and impacts approximately 90% of adolescents with most youth likely to have some form of skin breakout.[13, 33, 64] Acne also persists into early adulthood with approximately one quarter of people likely to struggle with acne at 25 years of age, and for some, it can endure into middle adulthood, impacting 20-30% of people between the ages of 20 and 40.[13, 65] Though acne often begins in adolescence, some people experience onset in adulthood.[39] Often due to hormone cycles, 75% percent of adult acne sufferers are girls and women.[13, 39] Further, one in five people who have even mild acne can have permanent scarring (e.g., skin indentations, hyperpigmentation), which can make acne problematic even after it has been treated, and in some cases, stigmatizing across the lifespan.[66-68] Unfortunately, acne appears on the face in 99% of cases, making it extremely visible to others and a difficult problem to conceal, especially for boys and men.[13, 69, 70] Acne also affects other areas of the body with 50% of cases appearing on the neck, back, and arms.[13, 70] One study showed that people with facial acne suffered worse body image disturbance than those with body acne, underlining that psychosocial distress may be exacerbated as acne visibility increases.[71]

The causes and severity of acne can vary from person to person but are often related to a combination of biological (e.g., hormone levels, genetics, sebum production, medications)[12] and environmental (e.g., sweat, cosmetics, irritation of clothing/gear, stress) factors.[33, 71] With multiple factors conducive to acne onset, it is difficult for physicians to chart its course and determine how it may change over time for a given individual.[10] Despite this complex course, acne severity is generally classified using a three-part system that includes *mild* (i.e., a few small pustules near skin surface), *moderate* (i.e., multiple pustules or blackheads with inflammation across larger surface area), and *severe* (i.e., cysts or nodules and strong inflammation in infected

area).[13] Severe acne can cause soreness, swelling, and bleeding, making pain and discomfort challenging symptoms of this condition.[10, 12, 33]

Interestingly, objective acne severity rated by physicians or objective grading scales do not reliably align with the psychosocial experience of the acne sufferer.[16, 73, 74] Indeed, researchers [75-77] have shown that it is often the subjective or self-report rating of acne that correlates with psychosocial difficulty, thus patient distress is not always easily identified based on acne symptoms.[78] This is of concern given that researchers have also reported that non-psychiatric medical physicians have low accuracy in the identification of mental health problems which may leave disorders such as depression or anxiety unnoticed for physical complaints like acne.[79] Qualitative investigations of patients with skin diseases (i.e., acne, psoriasis, and eczema) have also shown that they feel misunderstood by physicians when it comes to their psychological impairment and often think doctors are apathetic to the emotional burden of their experience.[80] Although this is not the case for all, it is important to acknowledge the patient-practitioner discrepancies that can leave the psychosocial burden of acne undetected, and thereby unaddressed for its sufferers. One study also showed that use of an acne disability index assisted to identify patients with poor self-image, a potential indicator of psychosocial difficulty.[81] Combining such measures with mental health assessments may facilitate quicker identification of those at risk.

Current evidence supports the prompt treatment of acne to reduce its psychosocial burden.[82] Acne treatments take several forms due to its complex etiology, though primary interventions for both sexes include combinations of topical retinoids, benzoyl peroxides, and antibiotics.[10] In more severe cases, isotretinoin (e.g., Accutane) may be prescribed.[83] For women, combined hormonal contraceptives are also effective in treating low to moderate acne.[84] Nonetheless, acne is a common[12] and often prolonged skin condition[13] characterized by high variability in its etiology[10], presentation, and disease course[10], making it a nuanced physical condition that unfolds dynamically over time and is associated with subclinical features[85] and clinical diagnoses of taxing disorders like depression and anxiety.[42]

Sociocultural Appearance Ideals

To best contextualize why acne may be so distressing to young adults, it is important to understand the broader sociocultural context in which modern young adults develop in societies. Researchers have noted that young adults are embedded within a Westernized appearance

culture[86], whereby adolescents and young adults engage in a high volume of appearance-based conversations[87] and are consistently exposed, both directly and indirectly, to sociocultural appearance ideals through media and socialization.[88-90] Sociocultural appearance ideals prescribe social standards for outward appearance and apply societal pressure to conform to narrow definitions of what is considered "attractive", "desirable", and "beautiful". [86, 91] Consequently, it is not surprising that young adults with acne commonly report psychological maladjustment such as self-consciousness, low self-esteem, depression, and anxiety, because the typical presentation of acne (i.e., redness and inflammation) is a marked departure from the commonly encountered appearance ideal of "clear skin". [3, 91]

Entirely clear skin, although non-existent, is a prominent appearance ideal that has been incessantly promoted in the media and beauty industry across the globe. According to the world's leading cosmetic brand, L'Oréal, skincare was the largest business segment in 2021 and comprised nearly 42% of their global beauty market.[93] With a massive platform and notable consumer market, the cosmetic and fashion industries along with social media influencers, celebrities, and Hollywood productions have largely broadcast the narrative that a youthful, blemish-free face belongs to the happiest, most successful, and popular person (e.g., celebrity endorsements of Proactiv, Rihanna of Fenty Beauty, Jennifer Anniston promotion of Aveeno), which distinctly tie skin appearance to valued psychosocial rewards.[94-96] In a qualitative study of 26 Australian people ranging from 10 to 52 years old, Magin et al. (2011) found that participants were aware of the discrepancy between themselves and the media's portrayal of clear skin.[97] Moreover, these participants acknowledged that this awareness led them to draw social comparisons that negatively impacted their self-perceptions.[97]

Conversely, those with skin diseases and acne are more often portrayed as malicious, unattractive, or unpopular (e.g., A witch with green skin and a wart on the nose, Leo Balmudo or "Craterface" in the film Grease).[98] Interestingly, Ritvo et al. (2011)[99] exemplified this appearance narrative in their study when they showed a nationally representative sample of American teens and adults (N = 2008; ages 13-17 and 18+), images of peers with and without facial acne. Participants consistently assigned lower ratings of several socially valued traits such as intelligence, confidence, popularity, and creativity to images with facial acne compared to the same image without facial acne.[99] Importantly, images with facial acne were also more often rated as introverted and shy, boring, lonely, stressed, and unhealthy.[99] This is important to note

given that teens with acne not only appear to be less likely to receive positive evaluations but also more likely to receive negative evaluations.[99] In another study, Jaeger et al. (2018)[100] independently assessed the impact of clear versus blemished skin on trait impressions (i.e., trustworthiness, competence, attractiveness) in a sample of 203 college students from the Netherlands. The blemished skin condition consistently had a strong negative effect on trait impressions when compared to baseline images, such that people with just mild acne were rated as less trustworthy, competent, and attractive.[100] In sum, failing to meet sociocultural appearance ideals may operate as a key force to foster psychosocial vulnerability amongst acne sufferers due to punitive social ramifications like negative appearance and character evaluations.[98-100] In turn, this may promote fertile ground for low-self-esteem, social withdrawal, and excessive worry about evaluation, key features of MDD, GAD, and SAD.[37]

Acne, Depression, and Anxiety

It is well documented that acne sufferers experience a high degree of clinical and subclinical symptoms of depression and anxiety (e.g., anger, suicidality, stress, low-self-esteem, self-consciousness, social withdrawal.[8, 23-25, 71, 85, 101, 102] For example, Do et al. (2009)[75] surveyed (N = 504) Korean middle school students aged 13 to 16 years old and found that earlier acne onset was positively associated with self-perceived stress, interpersonal and daily life disturbances, and depression scores, especially for young girls. As noted previously, this study found these psychosocial impairments were most strongly related to self-reported acne severity rather than objective acne severity, with girls self-reporting more severe acne than boys. Ozturk et al. (2013)[103] also reported significant social impairments in their comparison of clinical acne patients (n = 70, ages 16-30) with healthy age and sex matched controls (n = 50); those with acne reported lower scores on subscales of vitality and social functioning and higher scores on emotional difficulty than those without. The subthreshold region of a clinical disorder is a hazardous space for people to inhabit because there is lower likelihood that their symptoms will be recognized, yet a similar degree of psychosocial harm.[104-106] For example, Purvis et al. (2006)[107] conducted a cross-sectional survey analysis of self-reported acne and subclinical depression and anxiety in a sample of N = 9398 New Zealand youth aged 12-18 years. The authors accounted for age, gender, school ranking, and socioeconomic status in their logistic regression. "Problem acne" was reported by 14.1% of their sample and was related to higher odds ratios for depressive and anxiety symptoms, suicidal thoughts, and suicide attempts. The

association of acne and suicide attempts remained significant even after controlling for depression and anxiety symptoms.[107] Halverson et al. (2011)[20] also found greater suicidal ideation and impaired social relationships in their cross-sectional survey of Norwegian young adults with acne (i.e., $N = 3775$, 18-19 years old). Those with substantial acne reported low attachment to family and friends, not thriving in school, and less romantic and sexual involvement compared to those with little or no acne.[20] Without intervention there is high risk for those presenting with subclinical symptoms of depression and anxiety to enter the clinical disorder range, which appears to be the case for some with acne.[106] Indeed, clinical depression and suicidal ideation are distressing experiences not uncommon to those enduring acne.[19, 20, 107,108] Gupta and Gupta (1998) assessed the prevalence of depression and suicidal ideation in four types of dermatological patients (i.e., mild-moderate non-cystic facial acne $n = 72$, $M_{age} = 23.7$, alopecia, atopic dermatitis, and psoriasis).[19] Patients with non-cystic facial acne had the second highest depression rating next to psoriasis outpatients, with both groups showing average scores above the clinical cut-off.[19] Suicidal ideation showed a similar trend, with 5.6% of acne patients and 7.2% of psoriasis patients endorsing thoughts of suicide.[19] However, there were no sex differences in depression or suicidal ideation.[19] Halverson et al. (2011) also reported that nearly one-quarter of participants with substantial acne experienced suicidal ideation.[20] Further, in a multivariate model controlling for depression, family income, and ethnicity, Halverson et al. (2011) found that suicidal ideation remained significant among participants with substantial acne.[20] Suicidal ideation was twice as prevalent in girls with substantial acne compared to girls with little or no acne.[20] For boys with substantial acne, suicidal ideation was three-fold compared to boys with little or no acne.[20] As acne severity increases, it appears to confer risk for suicidal ideation, a distressing symptom by itself, and a key indicator of MDD.[20, 37]

Retrospective and archival studies have also illustrated higher prevalence and risk for clinical depression in acne patients.[109, 110, 111] Uhlenhake et al. (2010)[110] examined medical data in the U.S. and found that clinical depression was twice as high in patients with acne (8.8%) compared to the general population. When looking at individual age groups, most patients seen by a physician for acne were over the age of 18 (61.9%) and were women (65.2%).[110] Women with acne also showed double the prevalence of depression than men with acne, with 10.6% and 5.3% respectively.[110] This is in line with traditional depression rates that depict an approximate two to one female to male sex ratio.[37, 112] Across the world, Yang et al. (2014)[111] examined

records from the National Health Insurance database in Taiwan (N = 1,000,000) to assess sex differences in acne, major depression, and suicide using International Classification of Diseases-10 criteria. In general, diagnosis of depression was significantly higher in those with acne irrespective of sex, with an overall prevalence of 0.77% and 0.56% in controls. However, sex analysis revealed that women were at increased risk for major depression compared to men, with acne significantly contributing to this risk.[111] Contrary to Halvorsen et al. (2011), suicide was only slightly higher in those with acne but did not reach significance for this study.[20, 111] Finally, in a large retrospective cohort study, Vallerand et al. (2018)[110] examined N = 134, 437 individuals with acne and N = 1, 731, 608 (aged 7-50 years) using a UK primary care database. Vallerand et al. covaried age (young $\leq$ 19; adult > 19), sex, obesity, smoking and alcohol use, socioeconomic status, and medical conditions at baseline. Over a 15-year follow up, their study showed the risk for developing clinical major depression was 18.5% in patients with acne, compared to 12% in the general population.[110] This risk was highest within the first year of diagnosis then decreased. As in other studies, girls and young women carried the greatest depression risk and were more likely to suffer from acne.[110] In sum, clinical depression and suicidality appear to be concerning side-effects of acne, especially for young women.[19, 20, 107-111]

Unlike clinical depression and suicidal ideation, fewer studies have assessed the prevalence and relation of clinical anxiety with acne. Most studies include small cross-sectional group comparison methods and assess depression and anxiety concurrently (see Samuels et al., 2020 for review).[42] In addition, most of these studies have occurred in Middle Eastern regions such as Turkey and Egypt. In fact, 21 of the 42 studies reviewed in Samuels et al.'s (2020) meta-analysis were from these regions.[42, 113, 114] Nonetheless, most researchers have reported higher odds ratios of clinical anxiety and depression for patients with acne when compared to controls.[103, 115, 116] In one study, Yarpuz et al., (2008) compared 83 clinical acne patients between the ages of 15 and 40 years old with 58 age and sex matched controls and found that acne patients showed significantly higher average scores on depression and general anxiety than patients without acne.[116] Patients also tended to self-rate their acne as more severe compared to physician grading.[116] However, contrary to other studies[74, 75] no relation between self-rated acne and psychosocial impairment was reported.[116] This could be related to the wide age range (i.e., up to 40 years old), as the preoccupation with physical appearance is generally strongest in adolescence and decreases in adulthood.[34-36]

Using a slightly larger sample, Bez et al. (2011)[114] compared 140 clinical acne patients aged 15 to 33 years old (M = 20.75) with 98 controls. Social phobia was diagnosed in almost half of the acne patients (45.7%), but in less than one quarter of controls (18.4%). Acne patients had significantly higher total avoidance scores on measures of social anxiety and significantly more work and family disability.[114] Interestingly, measures of general anxiety and depression scores showed no significant differences between acne patients and controls.[114] This may suggest a stronger relation between acne and social anxiety rather than general anxiety. Comparably, Ozturk et al. (2013) also observed the largest group difference between clinically graded acne patients and controls on measures of social anxiety.[103] Further, when looking at the effects of acne severity, those with severe acne (i.e., nodules on face or body) had significantly higher total social anxiety scores compared to those with mild acne (< 20 facial lesions), depicting stronger social impairment in this group.[103] General depression and anxiety scores were still significantly higher in acne patients than controls, but the strongest difference was observed in social anxiety.[103] In another study, Salman et al. (2016)[115] compared vitiligo (n = 37) and acne patients (n = 37) to age and sex matched controls (n = 74) in Turkish young adults (>18 years of age). They collected self-reported and physician-rated symptoms and found the acne group reported higher total and subscale scores on social anxiety and depression compared to controls.[115] In contrast, in a larger scale Turkish community (n = 308) study, Aktan et al. (2000)[113] showed no statistical differences in average scores between acne patients and controls for anxiety or depression. There were also no observed differences based on acne severity or age, though similar to most studies, girls with acne reported higher anxiety scores than boys.[113]

The only prospective longitudinal study was conducted by Ramrakha et al. (2016)[21] and they reported data from the Dunedin Multidisciplinary Health and Development Study in New Zealand. In their population birth cohort study (n = 1037) that began data collection in 1975 (age 3) with follow ups every two years until the age of 15, then again at ages 18, 21, 26, 32, and 38, participants were evaluated on mental, physical, and psychosocial health, which included measures of depression and anxiety.[21] At age 21, participants were asked retrospectively if they had experienced "problem acne" starting at the age of 15 or later; this was continued until the last time point (i.e., age 38). [21] Their results showed that acne was consistently and significantly associated with higher odds ratios for anxiety at all time points, and significance persisted when controlling for confounds of sex, socioeconomic status, and previous psychiatric diagnoses. [21]

MDD diagnosis displayed a similar pattern but did not reach statistical significance. [21] Post-hoc tests indicated that the relation between acne and depressive symptoms was significant after controlling for the noted confounds, again highlighting the danger that people with acne may linger in the critical subthreshold region of MDD, leaving many problems undetected. [21] Compatible trends of anxiety and depression prevalence were reported by Dalgard et al. (2015)[6] such that in their large-scale study (N = 4994) of skin diseases, clinical anxiety (15.1%) was more prevalent than depression in patients with acne (5.7%). Ramrakha et al. (2016) [21] also reported no interaction effects based on sex or age, suggesting comparable effects across sexes and age groups, which is similar to some studies (e.g., Aktan et al., 2000)[113], though divergent from most (e.g., Samuels et al., 2020).[42] Given that Rhamrakha et al. (2016)[21] appears to be the only prospective longitudinal study in the literature, there is a need for improved study designs that account for variation in acne presentation and its psychosocial impact across development.

In their meta-analytic review, Samuels et al. (2020)[42] summarized that youth and adults with acne exhibit higher risk and rates of depression and anxiety than the general population. Unsurprisingly, this risk is not evenly shared. Girls and young women accrue the most risk for internalizing symptoms, while boys and men with acne appear more likely to contemplate suicide.[20, 111] Additionally, suicidality appears most prevalent in those with substantial acne,[20, 107] suggesting a relation between mental health symptoms and acne severity. Girls and women are also more likely to seek medical treatment for their acne[109] aligning with research that demonstrates girls and women generally report more appearance anxiety than boys and men.[117]

Further, due to the visible nature of acne and its relation to negative trait and appearance evaluations by peers, it seems logical that individuals with acne would suffer from social anxiety more than general anxiety symptoms because a core feature of social anxiety is the fear of negative evaluation.[37] However, there does appear to be increased general anxiety symptoms in those with acne, though the relation may be less pronounced.[103, 113, 114] Briefly, the studies reviewed here suggest higher prevalence and risk of depressive and anxiety symptoms and disorders in adolescents and adults with acne. However, notable methodological limitations in the aforementioned study designs preclude the determination of causal relations; namely their cross-sectional nature, retrospective assessments of acne and/or mental health problems, and the failure to control for prior mental health symptoms (a known predictor of current mental health).[37, 48, 58] Another notable gap is the failure to account for the use of combined hormonal

contraception and isotretinoin, regularly prescribed acne treatments that have been linked with depression and suicidal ideation.[118-121]

Hormonal Contraceptives, Isotretinoin, and Acne

The rapid and effective treatment of acne is essential to mitigate the damaging subclinical and clinical symptoms of depression and anxiety just reviewed.[82] Of note, some treatments for acne have been questioned on their safety when it comes to mental health side effects.[122] Isotretinoin is a well-known third-line treatment for severe acne that has been implicated in the development of internalizing symptoms including depression and suicidal ideation and behaviour.[122] Similarly, combined oral contraceptives (COC; e.g., Ortho Tri Cyclen) are often used to treat acne in women with no medical contraindications and have also been linked with depression and anxiety.[123, 124] Although isotretinoin and COC remain effective for many in reducing acne, their role in the presentation of internalizing side effects cannot be overlooked if acne treatment is to address all acne symptoms.

Broadly, COC are a class of hormonal contraceptive (HC) which typically contain varying ratios of the exogenous hormones oestrogen and progestin.[84] COC work to suppress the female body's natural hormone production (e.g., androgens), decrease sebum (i.e., oils), and by extension, diminish acne.[121] They are generally prescribed when topical treatments have been exhausted, if acne presentation corresponds with the menstrual cycle or if patients report struggles with oily skin.[124] COC may also be prescribed as a precursor to isotretinoin in women.[124] To date, there has been no clear link between HC use and internalizing symptoms identified and the literature largely reviews depressive rather than anxiety symptoms.[125]

Nevertheless, some subgroups (e.g., adolescent girls and women with previous psychiatric history) have been recognized as at risk of affective disturbance when using HC.[125, 126] For example, Skovlund et al. (2016)[62] assessed adolescents and women aged 15-34 years old at any point during a 14-year period. Depression incidence was measured using "redeemed prescription of antidepressant" and "first diagnosis of depression".[62] Of note, categorical cut-offs for depression like these should be interpreted with caution because they fail to capture many people suffering subclinical symptoms of depression and do not reflect the continuous nature of mental health. They reported that users of COC had a risk ratio of first antidepressant use of 1.2 compared to non-users.[62] When analyses were stratified by age, this risk increased to 1.8 for young women aged 15-19 years old, then decreased in women aged 20-34.[62] Depression risk

amongst COC users (1.2) was lower compared to other HC methods like the intrauterine system (1.4), vaginal ring (1.6), the patch (2.0), the implant (2.1), and the "depot" injection (2.7).[62] It is important to note that depression onset is known to increase markedly after puberty, especially in young women, which may explain some of the variation observed between age groups in Skovlund et al. (2016).[37, 62] More recently, a large-scale study by Lundin et al. (2022)[120] in a sample of (*n* = 739 585) Swedish women aged 15 to 25 years-old showed lower to equal risk for depression between COC users, non- and never- users. Marginal increases in depression risk were observed with women who used the patch, vaginal ring, implant, or intrauterine device.[120] Again, use of any HC was associated with increased risk for depression in women 15-19 years old when stratified by age. However, when stratified by type of HC, COC specifically showed no increase in depression.[120] In another study, Doornweerd et al. (2022) assessed general oral contraception (OC) use and internalizing symptom trajectories in a sample of (n = 178 at Wave 1 in 2006) Dutch girls who were followed from age 12-24 years old.[123] In this sample, those who reported using OC at some point had stable trajectories of depressive and anxiety symptoms compared to never-users who showed increasing trajectories in late adolescence, indicating possible mediating effects of HC on internalizing symptoms.[123] The results remained stable when covariates (e.g., first sexual debut) were added, though this study did not report information on OC type, limiting inferences in this area and about COCs specifically.[123] Generally, there appears to be varying risk for depressive symptoms that differ by age or type of HC, with COC use typically showing the least depressive risk.[62] Adolescent girls and young women experienced the highest depressive risk; though, this finding may be partially explained by traditional depression onset known to increase in this age group.[37] Physicians should actively consider the mental health contraindications reviewed here to ensure prudent administration of COC for acne, especially for developing young women.

Like COC, the relation between isotretinoin and depression has yet to be firmly established and some studies report conflicting results.[122, 127] The latest meta-analysis of 20 studies reported discrepant results between retrospective studies that assessed depression risk amongst isotretinoin users and prospective studies that assessed depression change (i.e., pre-and post-isotretinoin treatment).[128] In the retrospective studies, depression-risk was heightened amongst isotretinoin users, whereas in depression-change studies, results showed isotretinoin reduced depression symptoms post-treatment.[128] Another systematic review and meta-analysis

conducted by Huang and Cheng (2016) reported that 25 out of the 31 studies they assessed showed no significant association between low dose (0.5-1 mg/kg) isotretinoin and depression scores.[127] Further, 11 out of those 25 studies reported decreased depression scores and frequency.[127] In general, patients with acne had higher baseline depression scores, which suggests an independent link between depression and acne.[127] Their study did not assess anxiety symptoms.[127] Conversely, another systematic review suggested that while pooled statistical analyses remain hopeful, there are case studies of individuals that experience worsening depressive symptoms and suicidal behaviour after beginning treatment with isotretinoin .[61, 63, 122] These reviews have suggested a dose-response relation between isotretinoin and symptoms related to depression (e.g., low libido, weight loss) and stress the need for physicians to uniquely consider each patient's mental health history and biological risk factors prior to prescription of isotretinoin.[61]

Another review by Oliveira et al. (2018)[129] highlights that the studies that suggest this positive association between isotretinoin, depression, and suicide tend to be descriptive in nature (i.e., case reports, database studies, retrospective analyses) and thus are restricted in their power to deduce causal conclusions.[130] Nonetheless, Oliveira et al. (2018)[129] also advocate for the subset of individuals who may experience worsened internalizing symptoms upon starting isotretinoin treatment. [129] A new large-scale retrospective cohort study compared risk of nine psychiatric outcomes including depression, MDD, suicidal ideation, and suicide attempt in acne patients using isotretinoin (n = 75, 708) versus oral antibiotics (n = 75, 708).[131] Participants were matched based on sociodemographic and related comorbidities such as smoking. Isotretinoin dosage and psychiatric history were not co-varied. Patients using isotretinoin showed reduced depression risk and similar MDD risk to patients using antibiotics.[131] Risk for suicidal ideation was slightly elevated in the isotretinoin group, though suicidal behaviour was comparable between both treatment groups.[131] Patients using isotretinoin also showed reduced risk for other psychiatric outcomes such as post-traumatic stress disorder, anxiety, bipolar disorder, schizophrenia, and adjustment disorder.[131] This study showed similar or reduced mental health risk amongst two types of acne treatment groups which is consistent with other studies investigating similar outcomes (e.g., Kaymak et al., 2009)[132]; however, the absence of a control group does limit comparison to the general population.

The relation between isotretinoin, depression, and suicidal ideation and behaviour, has yet to be securely established due to a high degree of variation in outcome measurement, and a lack of prospective studies and randomized control trials.[82, 127] One notable issue with studying demonstrated links is that the temporal ordering has not been assessed. Thus, it is unclear if isotretinoin causes mental health problems or if mental health problems predate the use of isotretinoin. However, based on the most recent cross-sectional, meta-analytic, and large-scale database studies, the relation appears to be mostly neutral or beneficial with isotretinoin treatment ameliorating psychiatric symptoms for most.[128, 131] As such, swift treatment using COC or isotretinoin is recommended to reduce the psychosocial burden of acne. Despite discrepant opinions, all research urges the extensive baseline screening and on-going monitoring of depression and anxiety symptoms upon administration of these acne treatments.[122, 127, 128] Groups that appear to be most at risk for depressive symptoms and that should be monitored closely include adolescent girls and patients with personal or family history of mental health diagnoses.[128, 133]

Conclusion

In this narrative review we sought to integrate the literature on acne and mental health with a specific emphasis on three common internalizing disorders and their symptoms, MDD, GAD, and SAD. We used a sociocultural framework to conceptualize how acne may manifest internalizing symptoms for some sufferers and found several trends that may support the effective biopsychosocial treatment of acne. First, acne is a marked deviation from the sociocultural media narrative that actively promotes clear skin as a beauty norm and expectation for women and men. The vast nature of this narrative may generate an internal overvaluation of the personal and social significance of perfected skin amongst consumers.[134] Several researchers have shown that teens and adults with acne also suffer damaging psychosocial judgements about their personal hygiene, health, qualities, and skills.[98-100] Such scrutiny may manifest new or reinforce existing symptoms such as a negative self-view, self-consciousness, depressed mood, suicidal ideations, and marked fear of evaluation. This trend appears to be corroborated in the studies reviewed here. Symptoms of MDD, GAD, and SAD appear to be both more likely and more prevalent amongst youth and adults who have acne.[21, 42]

Second, the literature reveals important sex differences that may prove useful for physicians monitoring acne treatment. In general, girls and women appear to be at the highest

risk for internalizing symptoms if acne is present.[109-111, 132, 135] This is consistent with traditionally reported sex differences in internalizing disorders.[37] Of note, girls and women may experience more internalizing symptoms than boys and men when acne is perceived as low to moderate.[75, 136] This may be related to high levels of general and appearance anxiety reported by women and girls and exceptionally high beauty standards.[3, 90, 94-96] As acne severity increases, boys and men seem to accrue more risk especially for symptoms related to MDD such as suicidal ideation.[20] Boys and men also have reduced access to primary acne treatments such as COC and are less likely to use makeup to cover blemishes which may exacerbate internalizing symptoms. Thus, boys and men with severe acne should be screened and monitored carefully for depressive symptoms. Boys and men also appear to be less likely to seek treatment for their acne, thus regular discussions about skin hygiene during check-ups may be beneficial to reduce stigma. Importantly, both sexes appear to drift in the uncharted subclinical region of MDD, GAD, and SAD when suffering from acne (e.g., low self-esteem, anger, social withdrawal, poor body image).[8, 23-25 71, 85, 101, 102] This is concerning given that a large burden of disease can prevail despite not meeting diagnostic criteria for DSM-5 disorders.[48, 104, 105] Thus, all patients seeking treatment for their acne should be provided with mental health and acne disability screening assessments (e.g., Patient Health Questionnaire-9, General Anxiety Disorder-7, Social Phobia Inventory).[80, 137-140] Such questionnaires are widely available within the public domain and require little patient time to complete. Despite inconclusive findings on the relation between COC and mental health, internalizing symptoms should be monitored closely to prevent symptom exacerbation when COC are prescribed, especially in teenage girls with acne.

Third, many studies have focused on GAD symptoms and diagnosis using Hospital Anxiety and Depression Scale or the Beck Anxiety Inventory.[42] However, large differences between controls and clinical acne patients were observed in studies that included SAD in their analyses, over and above GAD in some cases.[103, 114, 115] With fear of social pressure and evaluation as probable theoretical forces underlying acne and its relation to internalizing symptoms, longitudinal studies exploring SAD in-depth may shed light on the relation between acne and internalizing disorders.[141]

Finally, as Natsuaki and Yates (2021)[60] noted in their review, developmental approaches are lacking from the acne and mental health literature. This is a notable caveat because acne is known to vary in its incidence and presentation across the life span for women and men and

show a similar developmental course to internalizing symptoms.[12, 40, 42, 69, 85] Acne increases in prevalence after puberty and into young adulthood, which is similar to MDD, GAD, and SAD, though SAD often emerges slightly earlier in childhood.[10, 37] Of the studies reviewed here, only one (Ramrakha et al., 2016)[21] considered the developmental nature of acne, anxiety, and depression using a longitudinal approach. Prospective statistical methods that account for acne and its relation to mental health across time, and acne and its relation to mental health within the same time point have not yet been conducted. Therefore, longitudinal studies that include at least three time points, explore sex differences, use psychometrically sound assessments for MDD, GAD and SAD, and control for prior and concurrent mental health symptoms are needed. These methods will provide a clearer picture for physicians by highlighting the individuals who are most vulnerable to psychosocial harm because of acne. That is, when, how, and for whom, is acne likely to adversely impact psychosocial health across development. Such research will reinforce the need for a holistic and encompassing biopsychosocial treatment approach for this widespread and developmentally meaningful condition.

The findings of our review support the rapid provision of available acne treatments to effectively protect against symptoms of depression and anxiety that appear to plague many acne suffers. Physicians can take several steps to minimize the psychosocial impact of acne, which include: carefully attending to mental health contraindicators such as family or personal history of mental health with detailed intake and screening tools, provide patients with psychoeducation regarding the link between acne and depressive and anxiety symptoms, normalize insecurities related to acne, use measurement based care to monitor mental health changes throughout acne treatment, especially when COC or isotretinoin are prescribed, schedule appropriate follow ups, and facilitate patient access to third party practitioners such as dermatologists and mental health clinicians to support the comprehensive and safe management of all acne symptoms, including psychosocial health.

References

1. Gallo RL. Human skin is the largest epithelial surface for interaction with microbes. *J Invest Dermatol.* 2017;137(6):1213-1214.
2. Little AC, Jones BC, Debruine LM. Facial attractiveness: Evolutionary based research. *Philo Trans of the R Soc Lon B, Biol Sci.* 2011;366(1571):1638-1659.
3. Jack ER, Schyns PG. The human face as a dynamic tool for social communication. *Curr Biol.* 2015;14(25): R621-R634.
4. Bridgman AC, Fitzmaurice C, Dellavalle RP et al. Canadian burden of skin disease from 1990 to 2017: Results from the global burden of disease 2017 study. *J Cutan Med Surg.* 2020;24(2):161–173.
5. Bowe WP, Doyle AK, Crerand CE, Margolis DJ, Shalita AR. Body image disturbance in patients with acne vulgaris. *J Clin Aesthet Dermatol.* 2011;4(7):35–41.
6. Dalgard FJ, Gieler U, Tomas-Aragones L et al. The psychological burden of skin diseases: A cross-sectional multicenter study among dermatological out-patients in 13 European countries. *J Invest Dermatol.* 2015;135(4):984–991.
7. Beisert M, Pilarczyk K, Zakrzewska M, Pawlaczyk M. Sexual satisfaction and self-esteem in women with acne. *J Cosmet Dermatol.* 2020;19(7):1768-1773.
8. Hazarika N, Archana M. The psychosocial impact of acne vulgaris. *Indian J Dermatol*. 2016;61(5):515-520.
9. Mallon E, Newton JN, Klassen A, Stewart-Brown SL, Ryan TJ, Finlay AY. The quality of life in acne: A comparison with general medical conditions using generic questionnaires. *Br J Dermatol*. 1999;140(4):672–676.
10. Feldman S, Careccia RE, Barham KL, Hancox J. Diagnosis and treatment of acne. *Am Fam Physician*. 2004;69(9):2123-2130.
11. Zaenglein AL. Acne vulgaris. *N Engl J Med*. 2018;379(14): 1343-1352.
12. Bhate K, Williams HC. Epidemiology of acne vulgaris. *Br J Dermatol*. 2012;168:474-85.
13. Canadian Dermatology Association. Acne. 2021. https://dermatology.ca/public-patients/skin/acne. Accessed October 20, 2021.
14. Vos T, Flaxman AD, Naghavi M et al. Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990–2010: A systematic analysis for the Global Burden of Disease Study 2010. *Lancet*. 2012;380(9859):2163-2196.

15. Magin PJ, Pond CD, Smith WT, Watson AB, Goode SM. A cross-sectional study of psychological morbidity in patients with acne, psoriasis and atopic dermatitis in specialist dermatology and general practices. *J Eur Acad Dermatol Venereol.* 2008;22(12):1435-1444.
16. Niemeier V, Kupfer J, Demmelbauer-Ebner M, Stangier U, Effendy I, Gieler U. Coping with acne vulgaris: Evaluation of the chronic skin disorder questionnaire in patients with acne. *Dermatology.* 1998;196(1):108-115.
17. Dunn LK, O'Neill JL, Feldman SR. Acne in adolescents: Quality of life, self-esteem, mood, and psychological disorders. Dermatol Online J. 2011;17(1):1.
18. Tayel K, Attia M, Agamia N, Fadl N. Acne vulgaris: Prevalence, severity, and impact on quality of life and self-esteem among Egyptian adolescents. *J Egypt Public Health Assoc*. 2020;95(1):1-7.
19. Gupta MA, Gupta AK. Depression and suicidal ideation in dermatology patients with acne, alopecia areata, atopic dermatitis and psoriasis. *Br J Dermatol.* 1998;139(5):846–850.
20. Halvorsen JA, Stern RS, Dalgard F, Thoresen M, Bjertness E, Lien L. Suicidal ideation, mental health problems, and social impairment are increased in adolescents with acne: A population-based study. *J Invest Dermatol.* 2011;131(2):363–370.
21. Loney T, Standage M, Lewis S. Not just 'skin deep': Psychosocial effects of dermatological-related social anxiety in a sample of acne patients. *J Health Psychol*. 2008;13(1):47-54.
22. Ramrakha S, Fergusson DM, Horwood LJ et al. Cumulative mental health consequences of acne: 23-year follow-up in a general population birth cohort study. *Br J Dermatol.* 2016;175(5):1079-1081.
23. Dalgard F, Gieler U, Holm JØ, Bjertness E, Hauser, S. Self-esteem and body satisfaction among late adolescents with acne: Results from a population survey. *J Am Acad Dermatol.* 2008;59(5):746-751.
24. Tan JK. Psychosocial impact of acne vulgaris: Evaluating the evidence. *Skin Therapy Letter*. 2004;9(7):1-9.

25. Wu SF, Kinder BN, Trunnell TN, Fulton, JE. Role of anxiety and anger in acne patients: A relationship with the severity of the disorder. *J Am Acad Dermatol.* 1988;18(2):325-333.
26. Lasek RJ, Chren MM. Acne vulgaris and the quality of life of adult dermatology patients. *Arch Dermatol.*1998;134(4):454-458.
27. Pruthi GK, Babu N. Physical and psychosocial impact of acne in adult females. *Indian J Dermatol.* 2012;57(1):26–29.
28. Murray CD, Rhodes K. 'Nobody likes damaged goods': The experience of adult visible acne. *Br J Health Psychol.* 2005;10(2):183-202.
29. Yang YC, Tu HP, Hong CH et al. Female gender and acne disease are jointly and independently associated with the risk of major depression and suicide: A national population-based study. *BioMed Res Int.* 2014;504279.
30. Fellowes H, Billewicz W, Thomson A. Is acne a sign of normal puberty? A longitudinal study. *J Biosoc Sci.* 1981;13(4):401-407.
31. Kilkenny M, Stathakis V, Hibbert ME, Patton G, Caust J, Bowes G. Acne in Victorian adolescents: Associations with age, gender, puberty and psychiatric symptoms. *J Paediatr Child Health.* 1997;33(5):430-433.
32. Marceau K, Ram N, Houts RM, Grimm KJ, Susman EJ. Individual differences in boys' and girls' timing and tempo of puberty: Modeling development with nonlinear growth models. *Dev Psychol.* 2011;47(5):1389–1409.
33. American Dermatology Association. Acne clinical guideline. 2021. https://www.aad.org/public/diseases/acne; https://www.aad.org/media/stats-numbers
34. Harter S. Is self-Esteem only skin-deep? The inextricable link between physical appearance and self-esteem. *Reclaiming Children and Youth*. 2000;9(3):133-138
35. Elkind D. Egocentrism in adolescence. *Child Dev.*1967;38(4):1025-1034.
36. Somerville, LH. The teenage brain: Sensitivity to social evaluation. *Curr Dir Psychol Sci* 2013;22(2):121-127.
37. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 5th ed. Washington, D.C. 2013.

38. Avenevoli S, Swendsen J, He JP, Burstein M, & Merikangas, KR. Major depression in the national comorbidity survey-adolescent supplement: Prevalence, correlates, and treatment. *J Am Acad Child Adolesc Psychiatry.* 2015;54(1):37-44.
39. Rocha MA, Bagatin E. Adult-onset acne: Prevalence, impact, and management challenges. *Clin Cosmet Invest Dermatol.* 2018;11:59-69.
40. Gollnick HP, Finlay AY, Shear N, Global Alliance to Improve Outcomes in Acne. Can we define acne as a chronic disease? If so, how and when? *Am J Clin Dermatol.* 2008;9(5): 279-284.
41. Skroza N, Tolino E, Mambrin A, et al. Adult acne versus adolescent acne: A retrospective study of 1,167 patients. *J Clin Aesthet Dermatol.* 2018;11(1):21–25.
42. Samuels DV, Rosenthal R, Lin R, Chaudhari S, Natsuaki MN. Acne vulgaris and risk of depression and anxiety: A meta-analytic review. *J Am Acad Dermatol.* 2020;83(2):532–541.
43. Global Health Data Exchange. 2019. https://ghdx.healthdata.org/gbd-results-tool?params=gbd-api-2019-permalink/26fefed9b7933b26bdc9b140411bc63a
44. Whiteford HA, Degenhardt L, Rehm J et al. Global burden of disease attributable to mental and substance use disorders: Findings from the Global Burden of Disease Study 2010. *Lancet.* 2013;382(9904):1575-1586.
45. Racine N, McArthur BA, Cooke JE, Eirich R, Zhu J, Madigan S. Global prevalence of depressive and anxiety symptoms in children and adolescents during COVID-19: A meta-analysis. *JAMA Pediatr.* 2021;175(11):1142-1150.
46. Santomauro D, Herrera AM, Shadid J. Global prevalence and burden of depressive and anxiety disorders in 204 countries and territories in 2020 due to the COVID-19 pandemic. *Lancet.* 2021;398(10312):1700-1712.
47. Friedrich MJ. Depression is the leading cause of disability around the world. *JAMA.* 2017;317(15):1517.
48. Krygsman A, Vaillancourt T. Elevated social anxiety symptoms across childhood and adolescence predict adult mental disorders and cannabis use. *Compr Psychiatry.* 2022; 115:152302

49. Lewinsohn PM, Clarke GN, Seeley JR, Rohde P. Major depression in community adolescents: Age at onset, episode duration, and time to recurrence. *J Am Acad Child Adolesc Psychiatry*. 1994;33(6):809-818.
50. Zisook S, Lesser I, Stewart JW et al. Effect of age at onset on the course of major depressive disorder. *Am J Psychiatry*. 2007; 164(10):1539–1546.
51. Weissman MM, Wolk S, Goldstein RB et al. Depressed adolescents grown up. *JAMA.* 1999;281(18):1707-1713.
52. La Greca AM, Harrison HM. Adolescent peer relations, friendships, and romantic relationships: Do they predict social anxiety and depression? *J Clin Child Adolesc Psychol.* 2005;34(1):49-61.
53. Angst J, Angst F, Stassen HH. Suicide risk in patients with major depressive disorder. The *J Clin Psychiatry.* 1999;60(2): 57-116.
54. Findlay L. Depression and suicidal ideation among Canadians aged 15 to 24. *Statistics Canada, Catalogue no.82-003-X Health Reports.* 2017;*28*(1): 3-11.
55. Moffitt H, Caspi A, Kim-Cohen J, Goldberg D, Gregory AM, Poulton R. Depression and generalized anxiety disorder: Cumulative and sequential comorbidity in a birth cohort followed prospectively to age 32 years. *Arch Gen Psychiatry.* 2007;64(6):651-660.
56. Tully PJ, Cosh SM, Baune BT. A review of the affects of worry and generalized anxiety disorder upon cardiovascular health and coronary heart disease. *Psychol Health Med*. 2013;18(6):627-644.
57. Lewinsohn PM, Olaya B, Seeley, JR. Anxiety disorders in adolescents and psychosocial outcomes at age 30. *J Affect Disord.* 2014;163:125-132.
58. Stein MB, Stein DJ. Social anxiety disorder. *Lancet*. 2008;371(9618):1115-1125.
59. Golchai J, Khani SH, Heidarzadeh A, Eshkevari SS, Alizade N, Eftekhari H. Comparison of anxiety and depression in patients with acne vulgaris and healthy individuals. *Indian J Dermatol.* 2010;55(4):352–354.
60. Natsuaki MN, Yates TM. Adolescent acne and disparities in mental health. *Child Dev Perspect.* 2021;15(1):37-43.
61. Bremner JD. Isotretinoin and neuropsychiatric side effects: Continued vigilance is needed. *J of Affect Disord Rep*. 2021;6:100230.

62. Skovlund CW, Mørch LS, Kessing LV, Lidegaard Ø. Association of hormonal contraception with depression. *JAMA Psychiatry*. 2016;73(11):1154-1162.
63. Wysowski DK, Pitts M, & Beitz J. Depression and suicide in patients treated with isotretinoin. *N Engl J Med.* 2001;344(6):460.
64. Sawyer SM, Azzopardi PS, Dakshitha W, Patton GC et al. The age of adolescence. The *Lancet Child Adolesc Health*. 2018;2(3):223-228.
65. Collier CN, Harper JC, Cafardi JA. The prevalence of acne in adults 20 years and older. J *Am Acad Dermatol.* 2008;58(1):56-59.
66. Cleveland Clinic. Acne. 2021. https://my.clevelandclinic.org/health/diseases/12233-acne
67. Dréno B, Tan J, Kang S et al. How people with facial acne scars are perceived in society: An online survey. *Dermatol Ther.* 2016;6(2):207-218.
68. Goodman GJ. Post-acne scarring: A short review of its pathophysiology. *Australas J Dermatol.* 2001;42(2):84–90.
69. Lynn DD, Umari T, Dunnick CA, Dellavalle RP. The epidemiology of acne vulgaris in late adolescence. *Adolesc Health, Med Ther*. 2016;7:13-25.
70. Mayo Clinic. Acne Symptoms and Causes, Diagnosis and Treatment. 2021. https://www.mayoclinic.org/diseases-conditions/acne/symptoms-causes/syc-20368047
71. Papadopoulos L, Walker C, Aitken D, Bor R. The relationship between body location and psychological morbidity in individuals with acne vulgaris. *Psychol, Health Med.* 2000;5(4):431-438.
72. Halvorsen JA, Braae Olesen A, Thoresen M, Holm JØ, Bjertness E, Dalgard F. Comparison of self-reported skin complaints with objective skin signs among adolescents. *Acta Derm Venereol.* 2008;88(6):573-577.
73. Mulder MM, Sigurdsson V, van Zuuren EJ et al. Psychosocial impact of acne vulgaris: Evaluation of the relation between a change in clinical acne severity and psychosocial state. *Dermatology.* 2001;203(2):124-130.
74. Do JE, Cho SM, In SI, Lim KY, Lee S, Lee ES. Psychosocial aspects of acne vulgaris: A community-based study with Korean adolescents. *Annuals Dermatol.* 2009;21(2): 125–129.
75. Féton-Danou N. Psychological impact of acne vulgaris. *Ann Dermatol Venereol.* 2010;137(2):S62–S65.

76. Yazici K, Baz K, Yazici AE, Köktürk A, Tot S, Demirseren D, Buturak V. Disease-specific quality of life is associated with anxiety and depression in patients with acne. *J Eur Acad Dermatol Venereol.* 2004;18(4):435-439.
77. Moss TP. The relationships between objective and subjective ratings of disfigurement severity, and psychological adjustment. *Body Image*. 2005;*2*:151–159.
78. Cepoiu M, McCusker J, Cole MG, Sewitch M, Belzile E, Ciampi A. Recognition of depression by non-psychiatric physicians: A systematic literature review and meta-analysis. *J Gen Internl Med.* 2008;23(1):25-36.
79. Magin PJ, Adams J, Heading, GS, Pond CD. Patients with skin disease and their relationships with their doctors: A qualitative study of patients with acne, psoriasis and eczema. *Med J Aust*. 2009;190(2): 62–64.
80. Oakley AM. The Acne Disability Index: Usefulness confirmed. *Australas J Dermtatol.* 1997;37(1):37–39.
81. Ellington E. Isotretinoin: Risk or benefit to mental health in youth? J *Psychosoc Nurs Ment Health Serv.* 2022;60(2):7-9.
82. Villani A, Nastro F, Di Vico F et al. Oral isotretinoin for acne: A complete overview. *Expert Opinion on Drug Safety.* 2022;21(8):1027-1037.
83. Słopień R, Milewska E, Rynio P, Męczekalski B. Use of oral contraceptives for management of acne vulgaris and hirsutism in women of reproductive and late reproductive age. *Prz Menopauzalny.* 2018;17(1):1-4.
84. Gallitano SM, Berson DS. How acne bumps cause the blues: The influence of acne vulgaris on self-esteem. *Int J Womens Dermatol.* 2017;4(1):12–17.
85. Calogero, RM, Boroughs M, Thompson JK. The impact of Western beauty ideals on the lives of women and men: A sociocultural perspective. In V.Swami & A.Furnham (Eds.), Body beautiful: Evolutionary and sociocultural perspectives. New York: Palgrave Macmillan; 2007. 259-298 p.
86. Jones DC, Crawford JK. The peer appearance culture during adolescence: Gender and body mass variations. *J Youth Adolesc*. 2006;35:243-255.
87. Patrick H, Neighbors C., Knee CR. Appearance-related social comparisons: The role of contingent self-esteem and self-perceptions of attractiveness. *Pers Soc Psychol Bull.* 2004;30(4):501-514.

88. Tiggemann M, Barbato I. “You look great!”: The effect of viewing appearance-related Instagram comments on women’s body image. *Body Image*. 2018;27:61-66.
89. Want SC. Meta-analytic moderators of experimental exposure to media portrayals of women on female appearance satisfaction: Social comparisons as automatic processes. *Body Image.* 2009;6(4): 257-269.
90. Buote VM, Wilson AE, Strahan EJ, Gazzola SB, Papps F. Setting the bar: Divergent sociocultural norms for women's and men's ideal appearance in real-world contexts. *Body Image.* 2011;8(4):322-334.
91. L’Oréal. L’Oréal Annual General Report. 2022. https://www.loreal-finance.com/en/annual-report-2021/cosmetics-market/
92. Brown Z, Tiggemann M. Celebrity influence on body image and eating disorders: A review. *J Health Psychol*. 2022;27(5):1233-1251.
93. Grabe S, Ward LM, Hyde JS. The role of the media in body image concerns among women: A meta-analysis of experimental and correlational studies. *Psychol Bull.* 2008;134(3):460–476.
94. Nelissen R, Meijers MH. Social benefits of luxury brands as costly signals of wealth and status. *Evol Hum Behav.* 2011;32(5):343–355.
95. Magin P, Adams J, Heading G, Pond D. ‘Perfect skin’, the media and patients with skin disease: A qualitative study of patients with acne, psoriasis and atopic eczema. *Aust J Prim Health.* 2011;17(2):181-185.
96. Subrt A, Wagner RF. Comparative depictions of acne vulgaris in movies and in animated television cartoons. *J Med Movies.* 2013;9(4):178
97. Ritvo E, Del Rosso JQ, Stillman MA, La Riche C. Psychosocial judgements and perceptions of adolescents with acne vulgaris: A blinded, controlled comparison of adult and peer evaluations. *BioPsychoSocial Med.* 2011;5(1):11.
98. Jaeger B, Wagemans FMA, Evans AM, van Beest I. Effects of facial skin smoothness and blemishes on trait impressions. *Perception.* 2018;47(6):608–625.
99. Hedden SL, Davidson S, Smith CB Cause and effect: The relationship between acne and self-esteem in the adolescent years. *J Nurs Pract.* 2008;4(8):595-600.
100. Lenczowski E, Lake EP. More than skin deep: The psychosocial aspects of acne vulgaris. *J Dermatol Nurses' Assoc.* 2018;10(1S):S23-S24.

101. Özturk DE, Bagcioglu E, Atalay F, Serdar Z. Anxiety, depression, social phobia, and quality of life in Turkish patients with acne and their relationships with the severity of acne. *Turk J Med Sci.* 2013;43:660-666.

102. Angold A, Costello EJ, Farmer EM, Burns BJ, Erkanli A. Impaired but undiagnosed. *J Am Acad Child Adolesc Psychiatry.*1999;38(2):129-137.

103. Cuijpers P, Smit F. Subclinical depression: A clinically relevant condition? *Tijdschr Psychiatr.* 2008;50(8):519–528.

104. Lee YY, Stockings EA, Harris MG et al. The risk of developing major depression among individuals with subthreshold depression: A systematic review and meta-analysis of longitudinal cohort studies. *Psychol Med.* 2019;49(1):92-102.

105. Purvis D, Robinson E, Merry S, Watson P. Acne, anxiety, depression and suicide in teenagers: A cross-sectional survey of New Zealand secondary school students. *J Paediatr Child Health*. 2006;42(12):793-796.

106. Cotterill JA, Cuniliffe WJ. Suicide in dermatological patients. *Br J Dermatol.* 2003;137(2):246-250.

107. Uhlenhake E, Yentzer BA, Feldman SR. Acne vulgaris and depression: A retrospective examination. *J Cosmet Dermatol.* 2010;9(1):59-63.

108. Vallerand IA, Lewinson RT, Parsons LM et al. Risk of depression among patients with acne in the U.K.: A population-based cohort study. *Br J Dermatol.* 2018;178(3):e194-e195.

109. Cyranowski JM, Frank E, Young E, Shear MK. Adolescent onset of the gender difference in lifetime rates of major depression: A theoretical model. *Arch Gen Psychiatry.* 2000;57(1):21-27.

110. Aktan S, Özmen E, Berna S. Anxiety, depression, and nature of acne vulgaris in adolescents. *Int J Dermatol.* 2000;39(5): 354-357.

111. Bez Y, Yesilova Y, Kaya MC, Sir A. High social phobia frequency and related disability in patients with acne vulgaris. *Eur J Dermatol.* 2011;21(5):756-760.

112. Salman KE, Topcuoglu V, Demircay Z. Social anxiety and quality of life in vitiligo and acne patients with facial involvement: A cross-sectional controlled study. *Am J Clin Dermatol.* 2016;17(3):305-311.

113. Yarpuz, A. Y., Saadet, E. D., Şanli, H. E., & Özgüven, H. D. Social anxiety level in acne vulgaris patients and its relationship to clinical variables. *Turk J Psychiatry*. 2008;*19*(1):29-37.
114. Zimmer-Gembeck M, Webb H, Farrell L, Waters A. Girls' and boys' trajectories of appearance anxiety from age 10 to 15 years are associated with earlier maturation and appearance-related teasing. *Dev Psychopathol.* 2018;30(1):337-350.
115. Lewis CA, Kimmig AS, Zsido RG, Jank A, Derntl B, Sacher J. Effects of hormonal contraceptives on mood: A focus on emotion recognition and reactivity, reward processing, and stress response. *Curr Psychiatry Rep.* 2019;21(11):115.
116. Li C, Chen J, Wang W, Ai M, Zhang Q, Kuang L. Use of isotretinoin and risk of depression in patients with acne: A systematic review and meta-analysis. *BMJ Open*. 2019;9(1):e021549.
117. Lundin C, Wikman A, Lampa E et al. There is no association between combined oral hormonal contraceptives and depression: A Swedish register-based cohort study. *BJOG.* 2022;129(6):917-925.
118. Trivedi MK, Shinkai K, Murase JE. A review of hormone-based therapies to treat adult acne vulgaris in women. *Int J Womens Dermatol.* 2017;3(1):44-52.
119. Bremner JD, Shearer KD, & McCaffery PJ. Retinoic acid and affective disorders: The evidence for an association. *J Clini Psychiatry.* 2012;73:37-50.
120. Doornweerd AM, Branje S, Nelemans SA et al. Stable anxiety and depression trajectories in late adolescence for oral contraceptive users. *Front psychiatry*. 2022;13:799470.
121. Harper JC. Should dermatologists prescribe hormonal contraceptives for acne?. *Dermatol Ther.* 2009;22(5):452-457.
122. Fruzzetti F, Fidecicchi T. Hormonal contraception and depression: Updated evidence and implications in clinical practice. *Clin Drug Investig.* 2020;40(12):1097-1106.
123. Schaffir J, Worly BL, Gur TL. Combined hormonal contraception and its effects on mood: A critical review. *Eur J Contracept & Reprod Health Care*. 2016;21(5):347-355.
124. Huang YC, Cheng YC. Isotretinoin treatment for acne and risk of depression: A systematic review and meta-analysis. *J Am Acad Dermatol.* 2017;76(6):1068–1076.e9.

125. Oliveira JM, Sobreira G, Velosa J, Telles Correia D, Filipe P. Association of isotretinoin with depression and suicide: A review of current literature. *J Cutan Med Surg.* 2018;22(1):58-64.

126. Strahan JE, Raimer S. Isotretinoin and the controversy of psychiatric adverse effects. *Int J Dermatol*. 2006;45(7):789-799.

127. Kridin K, Ludwig RJ. Isotretinoin and the risk of psychiatric disturbances: A global study shedding new light on a debatable story [published online ahead of print, 2022 Oct 20]. *J Am Acad Dermatol*. 2022;S0190-9622(22):02923-1.

128. Kaymak Y, Taner E, Taner Y. Comparison of depression, anxiety and life quality in acne vulgaris patients who were treated with either isotretinoin or topical agents. *Int J Dermatol. 2009*;48(1):41-46.

129. Kubota Y, Shirahige Y, Nakai IK, Katsuura J, Morique T, Yoneda K. Community-based epidemiological study of psychosocial effects of acne in Japanese adolescents. *J Dermatol.* 2010;37(7):617-622.

130. Gilovich T, Medvec VH, Savitsky K. The spotlight effect in social judgment: An egocentric bias in estimates of the salience of one's own actions and appearance. *J Pers Soc Psychol.* 2000;78(2):211-222.

131. Hassan J, Grogan S, Clark-Carter D, Richards H, Yates VM. The individual health burden of acne: Appearance-related distress in male and female adolescents and adults with back, chest, and facial acne. *J Health Psychol.* 2009;14(8), 1105-1118.

132. Kellett, S. C., & Gawkrodger, D. J. The psychological and emotional impact of acne and the effect of treatment with Isotretinoin. *Br J Dermatol.* 1999;140(2): 273–282.

133. Connor KM, Davidson JR, Churchill LE, Sherwood A, Foa E, Weisler RH. Psychometric properties of the Social Phobia Inventory (SPIN). New self-rating scale. Br J Psychiatry. 2000;176:379–386.

134. Kroenke K, Spitzer RL. The PHQ-9: A new depression and diagnostic severity measure. *Psychiatr Ann.* 2002;32:509-521.

135. Motley RJ, Finlay AY. Practical use of a disability index in the routine management of acne. *Clin Exp Dermatol.* 1992;17:1-3.

136. Spitzer, RL, Kroenke K, Williams JBW, Löwe B. Generalized Anxiety Disorder 7 (GAD-7). *APA PsycTests*. 2006.

137. Clark DM, Wells A. A cognitive model of social phobia. In RG Heimberg, MR Liebowitz, DA Hope, FR Schneier (Eds.), *Social phobia: Diagnosis, assessment, and treatment*. The Guilford Press. 1995. 69-93p.

Part 2: Acne, Depression, and Anxiety Symptoms in Young Adults

Abstract

Acne vulgaris is a widespread skin concern that has been implicated as a risk factor for symptoms and diagnoses of Major Depression (MDD) and Generalized Anxiety Disorder (GAD) across cultures, age groups, and sexes. However, few studies have examined this association across time and show conflicting results regarding the role of gender in this relation. Hormonal contraception is also a common treatment for women with acne and known to impact mood and anxiety levels in women, though few studies have controlled for it. Extant literature has also neglected to study Canadian demographics. Thus, we used logistic regression to examine the longitudinal relation between acne, depression, and anxiety symptoms and assessed the moderating role of gender. We also conducted a sub-analysis for women to examine the impact of hormonal contraceptives. Results showed that acne, depression, and anxiety were positively correlated within time. Acne predicted elevated anxiety symptoms when controlling for concurrent depression and gender (OR = 1.96, 95% CI [1.36-2.83]) at age 22 only. Across time, acne at age 22 predicted elevated anxiety symptoms at age 23 for men only (OR = 4.57, 95% CI [1.16-18.04]). There was no association between acne and depression or anxiety symptoms in our sub-analysis of women that controlled for hormonal contraceptives. Young men with acne should be screened carefully for anxiety symptoms, provided adequate psychoeducation about body-image and anxiety concerns, and offered prompt treatment for acne to reduce mental health burden. Additional longitudinal assessments of acne and internalizing symptoms are needed to explore its temporal precedence and varied impact across development.

Introduction

Acne vulgaris, hereafter referred to as “acne”, is one of the most universal and upsetting dermatological complaints seen by physicians (Canadian Dermatology Association [CDA], 2022). It is known to impact approximately 9.4 percent of the global population and carry the second highest burden of disease when it comes to skin disorders (Bhate & Williams, 2012; Karimkhani et al., 2017; Vos et al., 2012). In 2019, acne was reported to have an incidence of 117.4 million cases and prevalence of 231.2 million (Chen et al., 2022). Moreover, between 1990 and 2019 there has been nearly a 48% increase in disability adjusted life years related to acne (Chen et al., 2022). Nationally, acne affects nearly 20% or 5.6 million Canadians each year (CDA, 2022). Acne is well-known for its disruptive impact on physical appearance with recognizable symptoms such as redness, inflammation, closed comedones/pustules (i.e., whiteheads), open comedones (i.e., blackheads), papules, cysts, nodules, and excoriations that appear on the face and body (Feldman et al., 2004; Magin et al., 2008; Zaenglein, 2018). In addition to physical symptoms, individuals who suffer from acne report troubling psychosocial sequalae such as poor mental health (e.g., depression, anxiety, low self-esteem), social challenges (e.g., romantic and employment difficulties), and diminished quality of life (Dalgard et al., 2015; Hazarika & Archana, 2016; Karimkhani et al., 2017; Mallon et al., 1999). A recent U.S. report from the National Ambulatory Medical Care Survey showed that dermatologist and physician screening for mental health in patients presenting with acne is low (Taylor & Barbieri, 2020). They reported that from 2005 to 2016, an estimated 67.9 million medical visits for acne took place with 62.1% of people visiting a dermatologist and 33.1% seeing their regular physician. Of these cases, only 1.2 percent were screened for mental health, an extremely low number (Taylor & Barbieri, 2020). Dermatologists screened fewer patients (0.6%) than general doctors (2.2%) for mental health (Taylor & Barbieri, 2020). Despite widespread reports demonstrating harmful psychosocial side effects of acne, practical consideration of its mental health burden remains low. To effectively address acne, all symptoms, including mental health, must be considered and its psychosocial burden cannot be dismissed.

Acne in Teens and Young Adults

The physical and psychosocial burden of acne is primarily an affliction of adolescence and young adulthood, with 80-85% of sufferers falling between the ages of 12 and 24 years old (CDA; American Dermatology Association [ADA], 2022). Acne may lead to heightened levels

of emotional distress for this age group because adolescence and emerging adulthood are developmental periods associated with an increased emphasis on peer acceptance, social evaluation, physical appearance, and emerging identity (Elkind, 1967; Harter, 2000; Somerville, 2013). Acne's presence during these periods may exacerbate or confer symptoms of internalizing disorders (e.g., negative self-view or fear of evaluation) such as major depression, general, and social anxiety, that are known to peak at this time (American Psychiatric Association [APA], 2013). For example, higher levels of subclinical symptoms such as low self-esteem, anger, self-consciousness, and suicidal ideation are well documented in participants with acne compared to those without (Dalgard et al., 2008; Loney et al., 2008; Tan, 2004; Wu et al., 1988). Acne also negatively impacts socialization for teens and young adults with studies reporting evidence of decreased dedication to school, reduced intention to participate in extracurricular activities, and lower friendship attachment in acne sufferers (Dalgard et al., 2008; Loney et al., 2008; Tan, 2004; Wu et al., 1988). Conversely, other studies support that adults may suffer more psychosocial side-effects when it comes to acne because acne is not a developmental norm for this age group (Samuels et al., 2020).

Indeed, acne is also linked to psychosocial problems in middle and later adulthood (Samuels et al., 2020). Low self-esteem, appearance insecurity, high self-consciousness, and social withdrawal have been observed in adults with acne (Barankin & Dekoven, 2002; Hassan et al., 2009; Lasrek & Chen, 1998). Adults may be vulnerable to compounded stress because of the stigmatizing view that acne is a "teenage problem" and may have experienced long-drawn-out battles with acne. As such, studies have linked acne in adulthood to greater self-consciousness and feelings of insecurity (Hassan et al., 2009; Lasrek & Chen, 1998). In one study (n = 60; 17-53 years old), 97% of patients reported being bothered by facial acne and 87% described their appearance as the main concern; older adults reported worse quality of life than younger patients (Lasrek & Chren, 1998). These subclinical symptoms are linked to practical implications such as unemployment and sexual dissatisfaction which underscores the costly disruption acne can bring to critical domains of functioning and health for some sufferers (Hassan et al., 2009). Subclinical symptoms of MDD and GAD are important to consider because they can manifest similar psychosocial impairment to clinical symptoms, but often go undetected (Cuijpers & Smit, 2008; Konstantopoulou et al., 2020). The subclinical

psychosocial challenges for youth and adults with acne may also confer a pathway toward poor mental health at the clinical level, which appears to be the case for many (Samuels et al., 2020).

A recent quantitative review that assessed 42 cross-sectional studies from across the globe showed increased prevalence of clinical depression and anxiety in youth (i.e., ages 12-19) and adults (ages 19+) with acne compared to those without acne (Samuels et al., 2020). A significant association between acne and clinical depression was observed in both community and clinical samples, but the strongest relation emerged in the clinical adult sample ($r = .22$, $p <$. 00001; Samuels et al., 2020). Similar trends were observed for anxiety, as it was more prevalent in individuals with acne across all age groups ($r = .25$, $p < .00001$). However, significant associations were only observed within the clinical ($r = .32$, $p < .00001$) and not community samples ($r = .08$, $p > .05$). The relation between acne, depression, and anxiety was more pronounced in adults than in youth, validating that acne may indeed be acutely distressing for people that encounter it later in life due to developmental norms (Samuels et al., 2020). The included studies spanned several regions between the United States, Asia, and Africa, and implicate acne as a cross-cultural risk factor for poor mental health (Kohn et al. 2021). Of the 42 studies examined in this review, only one was from North America indicating a lack of knowledge about the impact of acne on the mental health of Canadians. Futher, there were no longitudinal studies in this review which emphasizes the shortage of studies exploring the relation between acne and mental health across developmental periods. In sum, acne appears to be uniquely linked to an increased prevalence of subclinical symptoms and clinical diagnoses of depression and anxiety in different age groups and cultures, though little is known about this relation in Canada and across time (Samuels et al., 2020; Natsuaki & Yates, 2021).

Internalizing Symptoms and Disorders

Depressive and anxiety disorders are prevalent and debilitating conditions that impact approximately 4.4% and 3.6% of the global population, respectively (World Health Organization [WHO], 2017). Depression is characterized by low mood, persistent sadness or feelings of worthlessness, anhedonia, altered appetite and sleep, fatigue and low energy, poor concentration, and suicidal thoughts and behaviour (APA, 2013). In 2010, MDD was among the top five leading causes of years lived with disability for Canadians (Institute for Health Metrics and Evaluation, 2010). Archival data from 2012 showed that nationally, 11% of young Canadians aged 15 to 24 reported depression in their lifetime and close to seven percent reported a

depressive episode in the last year (Findlay, 2017). GAD is often co-morbid with MDD and is characterized by excessive worries, trouble concentrating, inability to relax, irritability, and physical symptoms such as rapid heart rate or shortness of breath (APA, 2013, Moffitt et al., 2007). Findings from a 2018 survey of Canadian youth aged 12 to 24 showed that diagnosed anxiety disorders increased in prevalence from six percent in 2011 to approximately 13% in 2018 (Wiens et al., 2020). Research exploring the effects of the COVID-19 pandemic on mental health also highlight that symptoms of MDD and GAD have increased in prevalence or worsened for many young Canadians (Racine et al., 2021; Santomauro et al., 2021). Symptoms and diagnoses of MDD and GAD are independently and jointly associated with maladaptive outcomes in several domains such as poor academics, unemployment, substance use, declining physical health, and poor relationships, in adolescence and into adulthood (Brittain & Vaillancourt, 2023; Dooley et al., 1996; Hysenbegasi et al., 2005; Moffitt et al., 2007; Zhou et al., 2017). Subclinical levels of MDD and GAD manifest similar impairment to diagnoses, but remain neglected for many sufferers due to lack of measurement (Cuijpers & Smit, 2008; Lee et al., 2019; Unterrainer et al., 2018). It is valuable to assess all meaningful internalizing symptoms (subclinical and clinical) to capture the full scope of impaired individuals. The identification of risk factors for MDD and GAD is vital for the health of Canadians and an awareness of their impact among individuals with acne is key for the effective management of all acne symptoms.

In their recent narrative review, Hammill and Vaillancourt (2023) argued for the integration of the developmental psychology and dermatological fields to form a thorough comprehension of the psychosocial burden acne may carry throughout development. Sufficient cross-sectional and cumulative data implicate acne in the manifestation of poor mental health, irrespective of age, culture and ethnicity, and sex (Kohn et al., 2021). However, the relation between acne, depression, and anxiety symptoms, remains poorly understood since the extant literature has not sufficiently used longitudinal approaches. This is important because adolescence and early adulthood is a time when acne becomes most prominent and when mental health problems like MDD and GAD peak (ADA, 2022; APA, 2013; CDA, 2022). In sum, more research is needed to understand whether acne is a risk factor for symptoms of anxiety and depression across time. Specifically, longitudinal studies are required to substantiate current cross-sectional findings and help identify demographics that are susceptible to poor mental health because of acne. To date, there has been only one prospective longitudinal study, which

occurred in New Zealand (i.e., Ramrakha et al., 2016), that assessed the relation between acne, MDD, and GAD. Ramrakha et al. (2016) conducted a population birth cohort study based in New Zealand where they followed (n = 1037) participants from age three until age 38, starting in 1975. They contacted participants every two years until the age of 15 and then at three-year intervals until the final time point. Their data were part of the Dunedin Multidisciplinary Health and Development Study, which assessed participants on several physical and psychosocial health and well-being variables, and included diagnostic assessments of depression and anxiety (Ramrakha et al., 2016). Participants were asked at age 21 to recall if they had endured "problem acne" at age 15 or older. This question was included at each time point until the final year of study at age 38. Self-reports of problem acne were reliably and significantly related to elevated odds ratios for general anxiety at all time points. The significance of this association remained after controlling sex, socioeconomic status, and psychiatric history. Acne did not significantly predict higher odds ratios for MDD. When they controlled for the same confounds, a significant association between acne and depressive symptoms emerged. This highlights that acne sufferers may often hover in the subclinical region of a disorder, despite not meeting the clinical cut-off criteria. No interactions based on age or sex were observed and the authors noted that this likely speaks to the universal burden of acne and is in line with other studies (e.g., Aktan et al., 2000). Though, some studies contradict this finding and show that women and older age groups may bear more psychosocial risk than men and younger populations (e.g., Samuels et al. 2020; Yang et al., 2014). As a result, the primary aim of our study was to extend and replicate findings of Ramrakha et al. (2016) and assess the role of gender and the longitudinal relation between acne and symptoms of depression and anxiety in a community sample of Canadian young adults aged 20-23 years old.

Acne, Internalizing Problems, and Gender Differences

In general, acne appears to be problematic for young women and men. Dalgard et al. (2008) surveyed participants between the ages of 18 and 19 (n = 3775) and found moderate to severe acne was self-reported by 13% of girls and 14% of boys. Those with acne reported more depressive symptoms, lower self-attitude, feelings of uselessness, reduced pride and self-worth, and worse body dissatisfaction than their peers without acne (Dalgard et al., 2008). This finding was consistent for both genders. Moreover, after controlling for body mass index and depressive symptoms, acne explained low sense of pride and poor body image for both sexes, lower self-

worth for girls, and lower self-attitude for boys (Dalgard et al., 2008). Still, some studies highlight differences between genders indicating a more nuanced relationship (Do et al., 2009). Do et al. (2009) surveyed (N = 504) Korean middle school students aged 13 to 16 years old and found that earlier acne onset was positively associated with self-perceived stress, interpersonal and daily life disturbances, and depression scores, especially for young girls. This study found these psychosocial impairments were most strongly related to self-reported acne severity rather than objective acne severity, with girls self-reporting more severe acne than boys. Thus, girls with acne may be more likely to self-identify their acne as severe compared to boys (Do et al., 2009). This could be related to higher levels of general and appearance anxiety reported by women and girls, and high beauty standards (Cologero et al., 2007). Yang et al. (2014) reviewed the National Health Insurance database (N = 1,000,000) in Taiwan to assess sex differences in acne, major depression, and suicide. Depression diagnoses were significantly higher in those with acne irrespective of sex with an overall prevalence of 0.77% compared to 0.56% of controls. Results showed that women (6.1%) had an overall higher prevalence of acne than men (3.3%), and young women aged 7-12 years old had the highest prevalence of all age groups and genders (17.8%). In all age groups, women were found to have a higher likelihood of developing acne, and this risk remained high throughout development, whereas the risk for men decreased with age. Women were consistently at increased risk for major depression when compared to men and acne significantly added to this risk (Yang et al., 2014). Female gender and acne were also found to be risk factors for suicide (OR = 3.17, 95% CI [1.27-7.94]). Thus, in this large-scale prevalence study women appeared to be at greater risk than men to develop internalizing symptoms when acne is present. Importantly, disease severity was not captured in this study and thus could not be considered. Other studies show that boys and men may accrue more risk as acne severity increases, especially for symptoms related to MDD such as suicidal ideation. For example, Halverson et al. (2011) conducted a cross sectional survey of Norwegian young adults (i.e., N = 3775, 18-19 years old) and found that almost one-quarter of participants with substantial acne experienced suicidal ideation. Suicidal ideation was twice as prevalent in girls with substantial acne compared to girls with little or no acne and three-fold for boys with substantial acne compared to boys with little or no acne. In a multivariate model controlling for depression, family income, and ethnicity, Halverson et al. (2011) reported that suicidal ideation remained significant among participants with substantial acne. Retrospective and archival studies

also indicate that the majority of participants presenting to physicians for their acne are girls and women, suggesting that boys may be less likely to identify their acne as an issue and delay treatment (Uhlenhake et al., 2010; Vallerand et al., 2018). Boys and men are also unable to use hormonal contraception to regulate their skin and are less likely to cover blemishes with make-up, reducing options for acne management or concealment. Overall, acne is a concern for both genders, though some nuances remain. Girls appear to experience higher and more frequent psychosocial and appearance distress than boys when it comes to acne. As acne severity increases, boys may garner more risk for serious concerns such as strong suicidal ideation, a challenging symptom on its own, and a key marker of MDD. It is important to note that the typical gender ratio for female to male prevalence of depressive and anxiety disorders is approximately 2:1, thus we can generally expect to see young women with higher levels of these symptoms than men (Solomon & Herman, 2009).

The Current Study

Acne is a formative developmental experience that impacts the mental health of people worldwide. There is a growing body of evidence that demonstrates acne's association to psychosocial sequelae (e.g., major depression and anxiety disorders and symptoms), however, there remains a gap in the literature. The long-term and developmental impact of acne on internalizing symptoms has only been assessed in one study. In addition, extant literature as not clarified the role gender may play in this relation. We sought to answer two primary questions: (1) Does self-reported acne uniquely predict symptoms of depression and anxiety in young adulthood across time? and (2) Does gender moderate the relation between self-reported acne, depression, and anxiety symptoms across time? For these questions, we held three hypotheses: (H1) we expected a within time association between acne and internalizing symptoms, (H2) that acne would uniquely predict depression and anxiety symptoms (accounting for prior symptoms) across time, (H3) gender will moderate H2 such that women with acne would be more impaired than men with acne. Last, we conducted exploratory analysis of the role of hormonal contraception in this study because research regarding its impact on internalizing symptoms is conflicting.

Method

Procedure

This study used data from the McMaster Teen Study, a prospective longitudinal investigation of youth mental health, bullying, and development that began in 2008 when youth were in Grade 5 (T1) and has continued annually for 14 years until 2021 (T14). Participants were recruited from 51 randomly selected Southern Ontario schools. At T1, 875 students agreed to take part in the study and since then, 80% (n = 703) have continued to participate. Participants were offered two formats to complete the survey (online or paper) from T2 to T14; at T1 participants completed the survey in their classroom. Parental consent and student assent/consent were collected for the student survey portion. Students also participated in a structured clinical interview conducted by trained graduate students beginning at T9. Participants were compensated for survey and interview completion, which increased in value annually. Compensation for completing the survey and telephone interview consisted of a gift card worth $10 to $100, depending on the year of participation.

Participants

At Time 1, participants were on average, 10.91 years old (SD = 0.36). At Time 10 of the study 82.1 % of the sample was white, and 59.4% were girls. Data collected at Time 11 (T11; age 21) through Time 13 (T13; age 23) were used for the present study. Participants had an average age of 19.96 years old at Time 10, 20.96 years old at T11, 21.99 years old at Time 12 (T12), and 22.87 years old at T13 of the study.

Measures

Major Depression and Generalized Anxiety Symptoms. Major depression and general anxiety symptoms were assessed using the college version of Behaviour Assessment System for Children, Second Edition (BASC-2 SRP-COL; Reynolds & Kamphaus, 2004) from T11 until T13. The BASC-2 SRP-COL is a multidimensional measure that consists of 185 items to assess behaviour and self-perceptions of young adults aged 18-25. The BASC-2 SRP-COL contains eight subscales which include: depression, anxiety, attention problems, hyperactivity, somatization, interpersonal relations, self-esteem and atypicality. Participants endorse statements using a *true/false* format or rate the frequency using a four-point Likert scale (*Never*, *Sometimes*, *Often*, *Almost Always*). The depression subscale consists of 13 items, examples include, "Nothing feels good to me" and "I feel sad". The anxiety subscale consists of 13 items that assess general anxiety symptoms. Example items include *"I can never seem to relax"*, *"I worry but I*

don't know why". The BASC-II showed good reliability for the depression and anxiety scales which ranged from α = .90 - .94. Raw BASC-II scores were converted into t-scores and dichotomized into two groups, *not at risk = 0* and combined risk which included *subclinical and clinical symptoms = 1*. The subclinical symptoms were defined by a t-score cut-off range between 60-69. A t-score of 70 or above is considered clinically significant (Reynolds & Kamphaus, 2004). See Table 1.

Table 1.

Age, number of participants, mean BASC-11 score, standard deviation, and proportion of participants with subclinical and clinically significant depression and anxiety symptoms.

					Proportions	
	Age	N	Mean	Std. Dev	At risk	Not at Risk
Anxiety						
	20.96	395	15.97	9.40	31.3%	68.7%
	21.99	379	15.19	8.99	27.6%	72.4%
	22.87	356	15.23	8.81	29%	71%
Depression						
	20.96	390	5.95	6.36	15.7%	84.3%
	21.99	376	5.50	5.70	15.1%	84.9%
	22.87	351	5.49	5.90	16.2%	83.4%

Note. At risk denotes inclusion in the clinical and subclinical symptom category.

Acne. Acne was assessed at T11 (age 20.96) and T12 (age 21.99) of the study and the measure was constructed for the Mac Teen Study. The acne measure included 1 item to assess current acne levels (e.g., "*Do you currently have acne?*" *"Yes"* or *"No"*). When participants indicated that they had acne, participants rated the severity of their acne on a scale from zero *"Clear skin or no pimples"* to three *"Severe or a lot of pimples"*. There were no items to assess acne location in this measure. We used a median split to dichotomize acne into salient categories. Raw scores were converted into t-scores and collapsed into two categories *no acne and a little acne = 0* and *severe acne = 1* (See Table 2). This is similar to other longitudinal population cohort studies (e.g., Ramrakha et al., 2016) that have used dichotomisation to categorize acne and no acne.

Table 2.

Number of participants, mean score, standard deviation, and acne severity proportions.

				Proportions	
Age	N	Mean	Std. Dev	Severe Acne	Not Severe Acne
20.96	393	.62	.70	12.5%	87.5%
21.99	376	.58	.68	11.4%	88.6%

Note. Non-severe is collapsed scores of 0 and 1. Severe acne is collapsed scores of 2 and 3.

Hormonal Contraception. Hormonal contraception use was also assessed at T11 (age 20.96) and T12 (age 21.99) for women. We collected information about contraception via one question which asked "If female: Have you been taking any type of hormone-based birth control? If yes, please indicate the type of birth control you are currently using." Participants could select the following options: "No; birth control implant (e.g., Implanon, Nexplanon); birth control patch (e.g., Ortho Evra, Xulane); birth control pills (e.g., Alesse); birth control shot (e.g., Depo-Provera); or birth control vaginal ring (e.g., NuvaRing). Participants that indicated a type of birth control were coded as 1 and used for the analysis. Assessing differences between the type of contraception was beyond the scope of this study.

Analytic Plan

General bivariate correlations were conducted to assess within time-associations between continuous acne severity (i.e., full score range of 0-3) and dichotomized internalizing symptom risk (i.e., not at risk vs. combined subclinical/clinical risk). We then conducted a logistic regression analysis to assess the within time association of acne, depression and anxiety, and gender. We then performed an across-time logistic regression to test the difference between acne (i.e., little to no acne vs. severe acne) and the at risk (i.e., subclinical/clinical depression and anxiety or t-score above 60) and the not at risk group (t-score below 60). Gender was added into the across-time logistic regression model to assess symptom group membership for men and women independently. We controlled for self-reported use of hormonal contraception as part of the analysis for women. Previous depression and anxiety levels were also controlled at each time point. Regression models were created with the main effects model in one step and the interaction term added in the next step. In cases where the interaction was not statistically significant, the main effects model was reported.

Results

Missing Data

We used listwise deletion with logistic regression to remove participants with missing data. Skewness and kurtosis values were below the standard range (i.e., below 3 for skewness and below 10 for kurtosis; Kline, 2011). Little's Missing Completely at Random (MCAR) test was not statistically significant, $\chi 2(115) = 131.68$, $p > .05$, demonstrating that participants missing from the sample did not significantly differ from those included in the sample on measures of depression, anxiety, and acne.

Bivariate Correlations

Bivariate correlations between acne, depression, and anxiety symptoms were used to examine H1. Acne at age 21 was correlated with anxiety at age 21 ($r = .22$, $p < .000$), 22 ($r = .191$, $p < .001$) and, 23 ($r = .17$, $p < .003$). Acne at age 21 was also correlated with depression symptoms at age 21 ($r = .180$ $p < .001$), and 23 ($r = .14$, $p < .017$), but not 22. Acne at 22 showed similar results, with positive correlations with anxiety symptoms at age 21 ($r = .17$, $p < .003$), 22 ($r = .20$, $p < .0001$) and 23 ($r = .17$, $p < .003$). Acne at 22 was positively correlated with depression symptoms at 21 ($r = .12$, $p < .036$), and 23 ($r = .15$, $p < .012$), but not age 22. Acne at age 21 and 22 were positively correlated ($r = .52$, $p < .0001$). See Table 3 for correlations.

Table 3.

Bivariate correlations between acne (AC) and clinical and subclinical depression (Dep) and anxiety (Anx).

Variable	T11 AC	T12 AC	T11 Anx	T12 Anx	T13 Anx	T11 Dep	T12 Dep	T13 Dep
T11 AC	-	.516**	.215**	.191**	.169**	.180**	.097	.138**
T12 AC		-	.171**	.197**	.172**	.122*	.097	.146*
T11 Anx			-	.795**	.791**	.698**	.585**	.536**
T12 Anx				-	.805**	.582**	.688	.539**
T13 Anx					-	.574**	.677**	.680**
T11 Dep						-	.681**	.698**
T12 Dep							-	.751**
T13 Dep								-

Note. T11 (Time 11, age 20.96), T12 (T12, age 21.99), Time 13 (T13; age 22.87). *$p < .05$. **$p < .01$.

Logistic Regression Within Time

There were no significant within time associations between acne and depression symptoms at age 21, when controlling for concurrent anxiety symptoms and gender. There was also no association between acne and anxiety symptoms at age 21 when controlling for

concurrent depression and gender. Depression at age 21 predicted anxiety symptoms at age 21 (OR = 11.58, 95% CI [5.93-22.59]) and anxiety symptoms at age 21 predicted depression symptoms at age 21 (OR = 11.61, 95% CI [5.95-22.67] when controlling gender and concurrent depression and anxiety symptoms. Gender predicted anxiety symptoms at age 21 (OR = 1.51, 95% CI [1.15-1.97]) and age 22 (OR = 1.49, 95% CI [1.10-2.01]).

We found no statistically significant within time interactions between acne and gender at age 21 or 22. At age 22, acne predicted elevated anxiety symptoms (OR = 1.96, 95% CI [1.36-2.83]) when controlling for concurrent depression symptoms and gender. Depression symptoms at age 22 predicted anxiety symptoms at age 22 (OR = 14.30, 95% CI [7.12-28.74]) and anxiety symptoms at age 22 predicted depression symptoms at age 22 (OR = 14.49, 95% CI [7.18-29.24].

Logistic Regression Across Time

We found no significant across time association between acne and anxiety or depression symptoms at age 21 or 22. Depression (OR = 1.95, 95% CI [1.29-2.96]) and anxiety (OR = 3.82, 95% CI [2.76-5.29]) symptoms at age 21 predicted anxiety symptoms at age 22. Depression (OR = 4.24, 95% CI [2.80-6.43]) and anxiety symptoms (OR = 1.83, 95% CI [1.20-2.79]) at age 21 predicted depression symptoms at age 22. Depression but not anxiety symptoms at age 22 predicted depression symptoms at age 23 (OR = 5.38, 95% CI [3.27-8.87]. Depression (OR = 3.51, 95% CI [2.10-5.85]) and anxiety symptoms OR = 4.46, 95% CI [3.06-6.49] at age 22 predicted anxiety symptoms at 23.

The association between acne at 22 and anxiety symptoms at 23 when controlling for prior anxiety and depression symptoms depended on gender (β = 2.19, p = .037). We probed this finding by running the same logistic regression model separately for men and women. When controlling for depression and anxiety symptoms at age 22, acne at age 22 predicted elevated anxiety symptoms at age 23 for men only OR = 4.57, 95% CI [1.16-18.04]. There were no other significant across time associations when controlling for prior mental health and gender.

There was no association between acne and depression and anxiety symptoms in our sub-analysis of women that controlled for hormonal contraceptives. Depression and anxiety paths also remained stable. Depression (OR = 2.60, 95% CI [1.49-4.51]) and anxiety symptoms (OR = 4.28, 95% CI [2.83-6.46]) at age 21 predicted anxiety symptoms at age 22. Depression (OR = 3.88, 95% CI [2.34-6.45]) and anxiety (OR = 2.39, 95% CI [1.36-4.17]) symptoms at age 21

predicted depression symptoms at age 22. Depression (OR = 4.31, 95% CI [2.08-8.94]) and anxiety (OR = 4.82, 95% CI [3.02-7.68]) symptoms at age 22 predicted anxiety symptoms at age 23. Depression (OR = 4.74, 95% CI [2.68-8.39]) but not anxiety symptoms at age 22 predicted depression symptoms at age 23.

Discussion

We prospectively explored the longitudinal association of acne and MDD and GAD symptoms and the moderating role of gender. We also examined the role of hormonal contraceptives for women only. Our results showed support for the first hypothesis (H1) that acne was correlated with depression and anxiety concurrently and across time. This was as expected given the robust cross-sectional literature and descriptive findings that report positive associations between acne, depression, and anxiety symptoms (Hammill & Vaillancourt, 2023). Logistic regression supported this finding, such that acne at age 22 predicted risk for anxiety symptoms when controlling for gender and concurrent depression symptoms. This adds support to cross-sectional literature that reports acne as a risk factor for general anxiety symptoms (e.g., Samuels et al., 2020). Contrary to Samuels et al. (2020) that reported this association only in clinical acne patients, our results indicate an association in a community sample. However, we did separate our participant groups into dichotomous acne severity; thus, we interpret this extension to the community sample with caution. Samuels et al. (2020) also reported a significant relation between acne and depression, which our results do not support. Our result is surprising given the previous cross-sectional evidence (e.g., Hull & D'Arcy, 2005; Uhlenhake et al., 2010) that substantiates higher prevalence of depression and suicidal ideation (e.g., Halvorsen et al., 2011; Xu et al., 2021) in acne sufferers compared to controls. Overall, we view the lack of association between acne and depression in our study to be useful information that strengthens the need for studies that are able to control for concurrent mental health levels to discern associations more accurately. This finding also reinforces that cross-sectional literature that does not control for concurrent depression and anxiety levels may be skewed.

Our results showed partial support for acne as a predictor of internalizing symptoms across time (H2); however, we did expect that young women with acne would show increased risk for depression and anxiety symptoms (H3) compared to young men. We found that acne predicted anxiety symptoms across a one-year time period for men only when controlling for prior internalizing symptoms. This aligns with the results of Ramrahka et al. (2016) who also

found an across time association between acne and anxiety when controlling for previous psychiatric history. Their results, however, indicated no interaction with sex and suggested internalizing difficulties for both genders, which is incompatible with our results. There are several reasons why young men might show elevated anxiety compared to young women when it comes to acne. First, though women have higher prevalence rates of acne, some research has shown men report more severe acne (Aktan et al., 2000; Mohib, Zafar, & Syed, 2017). Severe acne may be more likely to confer mental health issues and could be one reason this relation appeared for young men and not young women. Young men are also more likely to experience acne across multiple visible body regions such as back, chest, and arms, which has been shown to contribute to higher psychosocial distress (Behnam et al., 2013; Papadopoulos et al., 2000). Men may also suffer stigma if they use make up to conceal their blemishes or lack knowledge about concealment products because most are marketed to women. In addition, they are unable to use hormonal contraceptives to manage acne symptoms, which is an effective and accessible treatment for young women and can mitigate negative mood (Mu et al., 2022). Finally, men seek treatment for their acne less often than women, which may lead to longer time periods with unmanaged acne symptoms and elevated anxiety that could contribute to why this finding persisted for one year (Uhlenhake et al., 2010; Vallerand et al., 2018). Our observed significant effects also emerged within age 22 and from age 22 to 23, which strengthens support for acne as a prominent stressor for emerging adults and when people age out of developmental norms (i.e., acne as a teen). However, we did not specifically test age and do not have a comparison group of adolescents to contrast these results.

In sum, our study supports that young men with severe acne may be more vulnerable to elevated anxiety symptoms than young women, and this finding persisted over a 1-year period. However, given that this was the only gender difference observed and other studies have reported either no gender differences (e.g., Ramrakha et al., 2016) or higher anxiety and risk for anxiety in girls and young women (e.g., Aktan et al., 2000; Yang et al., 2014), future research should continue to explore gender differences across time to verify these discrepancies. Importantly, our study showed hormonal contraception did not alter the association between acne and depression or anxiety symptoms in women. Because we found no significant associations between acne and depressive and anxiety symptoms for women in the general analysis, we did

not expect to see differences when we added hormonal contraception to the model, but verified this finding anyway.

Of note, there are studies that do not support a significant relation between acne and mental health. Aktan et al. (2000) reported in their study of adolescents aged 14-20 years old that acne patients did not differ from controls on measures of depression or anxiety. However, their sample consisted of younger participants where depression and anxiety levels are known to be high and acne is normative. Their study also used an objective grading scale to assess acne, whereas we used a self-rated measure. The use of objective versus self-rated acne measurement does appear to impact findings, such that objective and subjective ratings differ. This points toward the continued need for clarification of which variable appears first – acne or mental health challenges? Our study and that of Ramrakha et al. (2016) show support for the pathway that acne can independently lead to internalizing symptoms irrespective of prior mental health symptoms. In our study, this longitudinal association was present in men even when controlling for prior anxiety and depression. However, the psychodermatology field has described a vicious cycle whereby the relation between acne and poor mental health may be a bi-directional process between internalizing symptoms and biochemical processes (Bewley et al., 2021).

In general, our study is among the first to contribute to the body of longitudinal literature that explores acne and mental health and has added to the foundation of work that advocates for dermatology patients and their psychosocial experience. Although acne's impact on internalizing symptoms did not show a consistent effect across both time points, there is evidence for future studies to continue exploring this relation to settle discrepancies reported here and investigate gender differences in the mental health of acne sufferers.

Strengths, Limitations, and Future Directions

Our aim of this study was to contribute a baseline prospective longitudinal investigation to the field of psychodermatology and developmental psychology. This is the first study, to our knowledge, that prospectively assessed acne and mental health across time in Canadian young adults. This study measured acne across a two-year period and mental health across a three-year period which enabled us to consider the relation across a brief period of development that overlaps with the onset of internalizing symptoms. We used psychometrically sound measures of anxiety and depression symptoms and a self-reported acne measure which is known to reflect the

experience of the sufferer well (Do et al., 2009). We were able to assess gender differences and shed light on for whom acne is troubling.

Although the current investigation significantly contributed to the biopsychosocial understanding of acne in the context of development and mental health, there are limitations that must be addressed. Several environmental and biological factors are known to impact acne development and severity (e.g., higher BMI, smoking, genetics etc.; Sas & Reich, 2019; Zhang et al., 2021). We did not control for these variables due to time and measurement consistency constraints, thus some variance could be attributed to third party variables. Second, we were unable to assess social anxiety symptoms because we did not have a measure of social anxiety that corresponded with when acne data were collected, and thus, could not maintain measurement consistency across age groups. It would be useful to assess social anxiety specifically because the DSM-5 symptoms of social anxiety disorder (e.g., fear of evaluation, social withdrawal and avoidance) likely align more with the psychosocial challenges of acne than general anxiety, though symptom overlap can occur.

We did not assess the location of acne in this study, and evidence shows that psychosocial distress can vary by facial or body location (Papadopoulos et al., 2000). Additionally, we only used one item and a three point severity scale to assess acne. Valid and comprehensive measures that assess self-rated acne severity, along with other important factors such as location, duration, and onset would be useful to use for future studies. Another limitation that is important to note is the dichotomization of acne symptoms. We feel justified in using this approach because acne is typically a salient experience (i.e., you either had troublesome acne or not), and other studies have explored acne using similar categorical methods (e.g., Ramrakha et al., 2016). Nevertheless, this approach does not best reflect complex human experience and may reduce the capacity for detecting nuanced variance of acne symptoms and their relation with mental health. People who are anxious or depressed may rate their acne more severely due to the cognitive style that presents in these disorders (e.g., focusing on the negative, rumination, heightened self-focused attention) and may skew acne ratings, although we attempted to control for this by accounting for previous depression and anxiety levels. Further, we collapsed subclinical and clinical symptom categories to form an at-risk group that was inclusive of participants that hover in the subclinical region and experience meaningful impairment, but are often excluded from study results. We understand that this is also not representative of the

continuous nature of mental health and may result in skewed significance. Finally, our study sample consisted of primarily Caucasian demographic and results cannot be generalized to different ethnicities and races that we were unable to proportionately assess.

The field of psychodermatology continues to grow and explore the dynamic relation between our biological arousal and emotional systems and the skin. Understanding this relation in the context of acne would be helpful to target specific psychological stressors more directly (Hammill & Vaillancourt, 2023). Longitudinal research in this area should also explore the relation between acne and social anxiety symptoms, as psychosocial distress may be more related to social evaluation and appearance based judgements rather than general anxiousness. Future longitudinal research should consider evaluating location of acne, duration, and opportunity to conceal as potential variables of interest which may help target interventions for men and women. A developmental framework should be applied given that acne fluctuates across different ages and demographics, making its effects on mental health likely to change overtime. Longitudinal studies should also aim to include more than two time points for acne assessment and control for additional covariates to minimize confounding effects that we did not address here.

Conclusion

Researchers studying acne and its impact on mental health have advocated for longitudinal investigations to clarify its nuanced developmental relations (Natsuaki & Yates, 2021). This study addressed this concern and contributes to the biopsychosocial understanding and treatment of this prevalent and distressing condition for young Canadians. Although findings of this study should be interpreted with caution, the results have good face validity—acne and its relation to psychosocial distress is well established (Hammill & Vaillancourt, 2023). Accordingly, it is important that physicians attend to the emotional salience of acne for its sufferers and provide swift treatment to patients seeking remedies to alleviate their distress. Internalizing symptoms should be monitored in acne patients using available tools (e.g., PHQ9, GAD7) to protect against the development of poor psychosocial health. Timely referrals to mental health clinicians would support patients in managing any emotional symptoms that are beyond the physician scope of practice.

Mental health clinicians can support clients with acne by acknowledging acne as a salient developmental marker in their assessment or intake processes. History of acne or current acne

may influence key therapeutic targets such as core beliefs, body image, self-esteem, depressive or anxiety symptoms. Some studies have also associated acne with appearance based teasing and bullying, which are known to negatively impact mental and physical health (Magin et al., 2006; Rigby, 2003; Vaillancourt, Hymel & McDougall, 2013).

Adequate psychoeducation regarding stress responses in the body is also essential because sympathetic nervous system arousal is known to alter immune and inflammatory skin responses (Granstein & Luger, 2008; Poli, Dreno & Verschoore, 2001). Clinicians should do their best to pay detailed attention to the skin and body of their clients as an acne break out or other exacerbated skin issues may be related to mood disruption, chronic stress, or trauma (Chiu, Chon & Kimball, 2003; Picardi & Abeni, 2001). Practically, clinicians may consider a primary focus on stress reduction, emotion regulation, and de-escalation skills as tools for acne management. In sum, physicians and mental health clinicians must work together to validate the mental health burden of acne and promote a comprehensive and effective acne treatment that addresses its physical and psychosocial side-effects.

References

Aktan, S., Özmen, E., & Berna, S. (2000). Anxiety, depression, and nature of acne vulgaris in adolescents. *International Journal of Dermatology*, *39*(5), 354–357. https://doi.org/10.1046/j.1365-4362.2000.00907.x

American Dermatology Association. (2021). *Acne clinical guideline*. https://www.aad.org/public/diseases/acne; https://www.aad.org/media/stats-numbers

American Psychiatric Association. (2013). Diagnostic and Statistical Manual. 5th ed.

Barankin, B. & Dekoven, J. (2002). Psychosocial effect of common skin diseases. *Canadian Family Physician, 48*(4), 712-716. https://www.cfp.ca/content/48/4/712.short

Behnam, B., Taheri, R., Ghorbani, R., & Allameh, P. (2013). Psychological impairments in the patients with acne. *Indian Journal of Dermatology*, *58*(1), 26–29. https://doi.org/10.4103/0019-5154.105281

Bhate, K., & Williams, H. C. (2013). Epidemiology of acne vulgaris. *The British Journal of Dermatology, 168*, 474-85. https://doi.org/10.1111/bjd.12149

Brittain, H., & Vaillancourt, T. (2023). Longitudinal associations between academic achievement and depressive symptoms in adolescence: Methodological considerations and analytical approaches for identifying temporal priority. *Advances in Child Development and Behavior, 64*, 327–355. https://doi.org/10.1016/bs.acdb.2022.11.003

Calogero, R.M., Boroughs, M., Thompson, J.K. (2007). The impact of western beauty ideals on the lives of women: A sociocultural perspective. In: Swami, V., Furnham, A. (eds) The Body Beautiful. Palgrave Macmillan, London. https://doi.org/10.1057/9780230596887_13

Canadian Dermatology Association. (2021). *Acne.* https://dermatology.ca/public-patients/skin/acne

Chen, H., Zhang, T. C., Yin, X. L., Man, J. Y., Yang, X. R., & Lu, M. (2022). Magnitude and temporal trend of acne vulgaris burden in 204 countries and territories from 1990 to 2019: An analysis from the Global Burden of Disease Study 2019. *The British Journal of Dermatology*, *186*(4), 673–683. https://doi.org/10.1111/bjd.20882

Chiu, A., Chon, S. Y., & Kimball, A. B. (2003). The response of skin disease to stress: Changes in the severity of acne vulgaris as affected by examination stress. *Archives of Dermatology*, *139*(7), 897–900. https://doi.org/10.1001/archderm.139.7.897

Cuijpers, P. & Smit, F. (2008). Subclinical depression: A clinically relevant condition? *Tijdschr Psychiatry, 50*(8), 519–528.

Dalgard, F., Gieler, U., Holm, J. Ø., Bjertness, E., & Hauser, S. (2008). Self-esteem and body satisfaction among late adolescents with acne: Results from a population survey. *Journal of the American Academy of Dermatology*, *59*(5), 746–751. https://doi.org/10.1016/j.jaad.2008.07.013

Dalgard, F. J., Gieler, U., Tomas-Aragones, L., Lien, L., Poot, F., Jemec, G., Misery, L., Szabo, C., Linder, D., Sampogna, F., Evers, A., Halvorsen, J. A., Balieva, F., Szepietowski, J., Romanov, D., Marron, S. E., Altunay, I. K., Finlay, A. Y., Salek, S. S., & Kupfer, J. (2015). The psychological burden of skin diseases: A cross-sectional multicenter study among dermatological out-patients in 13 European countries. *The Journal of Investigative Dermatology*, *135*(4), 984–991. https://doi.org/10.1038/jid.2014.530

Do, J. E., Cho, S. M., In, S. I., Lim, K. Y., Lee, S., & Lee, E. S. (2009). Psychosocial aspects of acne vulgaris: A community-based study with Korean adolescents. *Annuals of Dermatology*, *21*(2), 125–129. https://doi.org/10.5021/ad.2009.21.2.125

Dooley, D., Fielding, J., & Levi, L. (1996). Health and Unemployment. *Annual Review of Public Health 17*:1, 449-465

Elkind, D. (1967). Egocentrism in adolescence. *Child Development, 38*(4), 1025–1034. https://doi.org/10.2307/1127100

Feldman, S., Careccia, R.E., Barham, K.L., & Hancox, J. (2004). Diagnosis and treatment of acne. *American Family Physician, 69*(9), 2123-2130.

Findlay, L. (2017) Depression and suicidal ideation among Canadians aged 15 to 24. *Statistics Canada, Catalogue no. 82-003-X*, Health Reports, *28*(1), 3-11. https://www150.statcan.gc.ca/n1/en/pub/82-003-x/2017001/article/14697-eng.pdf?st=b_h_07iu

Global Burden of Disease Collaborative Network. (2010). Global Burden of Disease, Injuries and Risk Factors Study Results by Cause 1990-2010. *Institute for Health Metrics and Evaluation (IHME).*

https://www.healthdata.org/sites/default/files/files/country_profiles/GBD/ihme_gbd_country_report_canada.pdf

Granstein, R. D., & Luger, T. A. (2008). Autonomic Effects on the Skin. In Neuroimmunology of the Skin (pp. 23–32). Springer Berlin / Heidelberg. https://doi.org/10.1007/978-3-540-35989-0_3

Halvorsen, J. A., Stern, R. S., Dalgard, F., Thoresen, M., Bjertness, E., & Lien, L. (2011). Suicidal ideation, mental health problems, and social impairment are increased in adolescents with acne: A population-based study. *The Journal of Investigative Dermatology*, *131*(2), 363–370. https://doi.org/10.1038/jid.2010.264

Hammill, C. & Vaillancourt, T. (2023). Acne and its association with internalizing problems. *Dermatological Reviews, (4)*5, 191-242. https://doi.org/10.1002/der2.181

Harter, S. (2000). Is self-Esteem only skin-deep? The inextricable link between physical appearance and self-esteem. *Reclaiming Children and Youth, 9(3), 133-138.*

Hassan, J., Grogan, S., Clark-Carter, D., Richards, H., Yates, V.M. (2009). The individual health burden of acne: Appearance-related distress in male and female adolescents and adults with back, chest, and facial acne. *Journal of Health Psychology, 14*(8), 1105-1118.

Hazarika, N., & Archana, M. (2016). The psychosocial impact of acne vulgaris. *Indian Journal of Dermatology*, *61*(5), 515–520. https://doi.org/10.4103/0019-5154.190102

Hull, P.R. & D'Arcy, C. (2005). Acne, depression, and suicide. *Dermatological Clinics, 23*(4), 665-674. https://doi.org/10.1016/j.det.2005.05.008

Hysenbegasi, A., Hass, S. L., & Rowland, C. R. (2005). The impact of depression on the academic productivity of university students. *Journal of Mental Health Policy and Economics*, *8*(3), 145.

Karimkhani, C., Dellavalle, R. P., Coffeng, L. E., Flohr, C., Hay, R. J., Langan, S. M., Nsoesie, E. O., Ferrari, A. J., Erskine, H. E., Silverberg, J. I., Vos, T., & Naghavi, M. (2017). Global Skin Disease Morbidity and Mortality: An Update From the Global Burden of Disease Study 2013. *JAMA Dermatology*, *153*(5), 406–412. https://doi.org/10.1001/jamadermatol.2016.5538

Kline, R.B. (2011) Principles and Practice of Structural Equation Modeling. 3rd Edition, The Guilford Press, New York.

Kohn, A. H., Pourali, S. P., Rajkumar, J. R., Hekmatjah, J., & Armstrong, A. W. (2022). Mental health outcomes and their association to race and ethnicity in acne patients: A population-based study. *Journal of the American Academy of Dermatology*, *87*(1), 140–142. https://doi.org/10.1016/j.jaad.2021.06.866Lasek, R. J., & Chren, M. M. (1998). Acne vulgaris and the quality of life of adult dermatology patients. *Archives of Dermatology*, *134*(4), 454–458. https://doi.org/10.1001/archderm.134.4.454

Konstantopoulou, G., Iliou, T., Karaivazoglou, K., Iconomou, G., Assimakopoulos, K., & Alexopoulos, P. (2020). Associations between (sub) clinical stress- and anxiety symptoms in mentally healthy individuals and in major depression: A cross-sectional clinical study. *BMC Psychiatry*, *20*(1), 428. https://doi.org/10.1186/s12888-020-02836-1

Lasek, R.J. & Chren, M. (1998). Acne vulgaris and the quality of life of adult dermatology patients. *Archives of Dermatology, 134,* 454-458. https://doi.org/10.1001/archderm.134.4.454

Lee, Y.Y., Stockings, E.A., Harris, M.G. et al. (2019) The risk of developing major depression among individuals with subthreshold depression: A systematic review and meta-analysis of longitudinal cohort studies. *Psychological Medicine, 49*(1), 92-102.

Loney, T., Standage, M., & Lewis, S. (2008). Not just 'skin deep': Psychosocial effects of dermatological-related social anxiety in a sample of acne patients. *Journal of Health Psychology*, *13*(1), 47–54. https://doi.org/10.1177/1359105307084311

Magin, P., Adams, J., Heading, G., Pond, D., & Smith, W. (2006). Psychological sequelae of acne vulgaris: Results of a qualitative study. *Canadian Family Physician*, *52*(8), 978–979.

Magin, P. J., Adams, J., Heading, G. S., & Pond, C. D. (2009). Patients with skin disease and their relationships with their doctors: A qualitative study of patients with acne, psoriasis and eczema. *The Medical Journal of Australia*, *190*(2), 62–64. https://doi.org/10.5694/j.1326-5377.2009.tb02276.x

Mallon, E., Newton, J. N., Klassen, A., Stewart-Brown, S. L., Ryan, T. J., & Finlay, A. Y. (1999). The quality of life in acne: A comparison with general medical conditions using generic questionnaires. *The British Journal of Dermatology*, *140*(4), 672–676. https://doi.org/10.1046/j.1365-2133.1999.02768.x

Moffitt, T. E., Harrington, H., Caspi, A., Kim-Cohen, J., Goldberg, D., Gregory, A. M., & Poulton, R. (2007). Depression and generalized anxiety disorder: Cumulative and sequential comorbidity in a birth cohort followed prospectively to age 32 years. *Archives of General Psychiatry*, *64*(6), 651–660. https://doi.org/10.1001/archpsyc.64.6.651

Mohib, A., Zafar, A., & Syed, H. (2017). Comparison study on frequency, severity, and risk factors of acne among male and female medical students. *Journal of Medical Science and Clinical Research, 5*(2), 18126-18132. https://dx.doi.org/10.18535/jmscr/v5i2.142

Mu, E., & Kulkarni, J. (2022). Hormonal contraception and mood disorders. *Australian Prescriber*, *45*(3), 75–79. https://doi.org/10.18773/austprescr.2022.025

Natsuaki, M.N. & Yates, T.M. (2021). Adolescent acne and disparities in mental health. *Child Development Perspectives, 15*(1), 37-43. https://doi.org/10.1111/cdep.12397

Papadopoulos, L., Walker, C., Aitken, D., & Bor, R. (2000). The relationship between body location and psychological morbidity in individuals with acne vulgaris. *Psychology, Health & Medicine*, *5*(4), 431-438.

Picardi, A. & Abeni, D. (2001) Stressful life events and skin diseases: Disentangling evidence from myth. *Psychotherapy and Psychosomatics, 70*(3) 118-136.

Poli, F., Dreno, B., & Verschoore, M. (2001). An epidemiological study of acne in female adults: Results of a survey conducted in France. *Journal of the European Academy of Dermatology and Venereology: JEADV*, *15*(6), 541–545. https://doi.org/10.1046/j.1468-3083.2001.00357.x

Racine, N., McArthur, B.A., Cooke, J.E., Eirich, R., Zhu, J., & Madigan, S. (2021). Global prevalence of depressive and anxiety symptoms in children and adolescents during COVID-19: A meta-analysis. *JAMA Pediatrics*, *175*(11), 1142–1150. doi:10.1001/jamapediatrics.2021.2482

Ramrakha, S., Fergusson, D. M., Horwood, L. J., Dalgard, F., Ambler, A., Kokaua, J., Milne, B. J., & Poulton, R. (2016). Cumulative mental health consequences of acne: 23-year

Reynolds, C. R., & Kamphaus, R. W. (2004). *Behavior assessment system for children* (2nd ed.). Bloomington, MN: Pearson Assessments.

Rigby, K. (2003). Consequences of bullying in schools. *Canadian Journal of Psychiatry, 48*(9), 583-590. https://doi.org/10.1177/070674370304800904

Samuels, D. V., Rosenthal, R., Lin, R., Chaudhari, S., & Natsuaki, M. N. (2020). Acne vulgaris and risk of depression and anxiety: A meta-analytic review. *Journal of the American Academy of Dermatology*, *83*(2), 532–541. https://doi.org/10.1016/j.jaad.2020.02.040

Santomauro, D., Herrera, A.M., Shadid, J., Zheng, P., Ashbaugh, C., Pigott, D.M., Abbafati, C., Adolph, C., Amlag, J.O., Aravkin, A.Y., Bang-Jensen, B.L., Bertolacci, G.J., Bloom, S.S., Castellano, R., Castro, E., Chakrabarti, S., Chattopadhyay, J., Cogen, R.M., Collins, J.K., ... Ferrari, A.J., (2021). Global prevalence and burden of depressive and anxiety disorders in 204 countries and territories in 2020 due to the COVID-19 pandemic. *The Lancet, 398*(10312), 1700-1712.

Sas, K., & Reich, A. (2019). High body mass index is a risk factor for acne severity in adolescents: A preliminary report. *Acta Dermatovenerologica Croatica: ADC*, *27*(2), 81–85.

Solomon, M. B., & Herman, J. P. (2009). Sex differences in psychopathology: Of gonads, adrenals, and mental illness. *Physiological Behaviour,* 97, 250–258. doi: 10.1016/j.physbeh.2009.02.033

Somerville, L. H. (2013). The teenage brain: Sensitivity to social evaluation. *Current Directions in Psychological Science*, *22*(2), 121-127. https://doi.org/10.1177/0963721413476512

Tan, J. K. (2004). Psychosocial impact of acne vulgaris: Evaluating the evidence. *Skin Therapy Letter*, *9*(7), 1–9. https://www.skintherapyletter.com/acne/psychosocial-impact/?amp=1

Taylor, M. & Barbieri, J.S. (2020). Depression screening at visits for acne in the United States, 2005-2016. *Journal of the American Academy of Dermatology, 83*(3), 936-938. doi:https://doi.org/10.1016/j.jaad.2019.12.076

Uhlenhake, E., Yentzer, B. A., & Feldman, S. R. (2010). Acne vulgaris and depression: A retrospective examination. *Journal of Cosmetic Dermatology*, *9*(1), 59–63. https://doi.org/10.1111/j.1473-2165.2010.00478.x

Unterrainer, J., Domschke, K., Rahm, B., Wiltink, J., Schulz, A., Pfeiffer, N., . . . Beutel, M. (2018). Subclinical levels of anxiety but not depression are associated with planning performance in a large population-based sample. *Psychological Medicine, 48*(1), 168-174. doi:10.1017/S0033291717002562

Vaillancourt, T., Hymel, S., & McDougall, P. (2013). The biological underpinnings of peer victimization: Understanding why and how the effects of bullying can last a

lifetime. *Theory into Practice*, *52*(4), 241–248. https://doi.org/10.1080/00405841.2013.829726

Vallerand, I.A., Lewinson, R.T., Parsons, L.M., Lowerison, M.W., Frolkis, A.D., Kaplan, G.G., Barnabe, C., Bulloch, A., & Patten, S.B. (2018). Risk of depression among patients with acne in the U.K.: A population-based cohort study. *The British Journal of Dermatology*, *178*(3), e194–e195. https://doi.org/10.1111/bjd.16099

Vos, T., Flaxman, A. D., Naghavi, M., Lozano, R., Michaud, C., Ezzati, M., ... & Harrison, J.E. (2012). Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990–2010: A systematic analysis for the Global Burden of Disease Study 2010. *The Lancet*, *380*(9859), 2163-2196. https://dx.doi.org/10.1016%2FS0140-6736(12)61729-2

Wiens, K., Bhattarai, A., Pedram, P., Dores, A., Williams, J., Bulloch, A., & Patten, S. (2020). A growing need for youth mental health services in Canada: Examining trends in youth mental health from 2011 to 2018. *Epidemiology and Psychiatric Sciences*, *29*, e115. https://doi.org/10.1017/S2045796020000281

World Health Organization, 2017. Depression and other common mental health disorders. Global Estimates. https://apps.who.int/iris/bitstream/handle/10665/254610/WHO-MSD-MER-2017.2-eng.pdf?s

Wu, S. F., Kinder, B. N., Trunnell, T. N., & Fulton, J. E. (1988). Role of anxiety and anger in acne patients: A relationship with the severity of the disorder. *Journal of the American Academy of Dermatology*, *18*(2), 325-333. https://doi.org/10.1016/s0190-9622(88)70047-x

Xu, S., Zhu, Y., Hu, H., Liu, X., Li, L., Yang, B., Wu, W., Liang, Z., & Deng, D. (2021). The analysis of acne increasing suicide risk. *Medicine*, *100*(24), e26035. https://doi.org/10.1097/MD.0000000000026035

Yang, Y. C., Tu, H. P., Hong, C. H., Chang, W. C., Fu, H. C., Ho, J. C., Chang, W. P., Chuang, H. Y., & Lee, C. H. (2014). Female gender and acne disease are jointly and independently associated with the risk of major depression and suicide: A national population-based study. *BioMed Research International*, 504279. https://doi.org/10.1155/2014/504279

Zaenglein, A. L. (2018). Acne vulgaris. *The New England Journal of Medicine*, *379*(14), 1343–1352. https://doi.org/10.1056/NEJMcp1702493c

Zhang, J. Z., Xiang, F., Yu, S. R., Luo, D., Li, T. T., & Kang, X. J. (2021). Association between acne and smoking: Systematic review and meta-analysis of observational studies. *Chinese Medical Journal*, *134*(15), 1887–1888. https://doi.org/10.1097/CM9.0000000000001286

Zhou, Y., Cao, Z., Yang, M., Xi, X., Guo, Y., Fang, M., Cheng, L., & Du, Y. (2017). Comorbid generalized anxiety disorder and its association with quality of life in patients with major depressive disorder. *Scientific Reports*, *7*, 40511. https://doi.org/10.1038/srep40511