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The Association of Affective Disorders and Facial Scarring: Systematic Review and Meta-Analysis.

Authors:

John. A. G. GibsonMBBcH, MRCS[1,2]*,Edward Ackling[3]*, Jonathan I. Bisson BM Dip Clin PSychotherapy FRCPsych DM[4], Thomas D. Dobbs BM BCh MA (Oxon) MRCS[2,3]; Iain. S. Whitaker MA Cantab, MBBChir, PhD, FRCS(Plast)[2,3].

1. Reconstructive Surgery & Regenerative Medicine Research Group, Institute of Life Science 2, Swansea University Medical School, Swansea, UK, SA2 8PP.

2. The Welsh Centre for Burns and Plastic Surgery, Morriston Hospital, Swansea, UK, SA6 6NL.

3. School of Medicine, Cardiff University, Cardiff, UK, CF14 4XN.

4. Division of Psychological Medicine and Clinical Neurosciences, Cardiff University, Cardiff, UK, CF14 4NX.

    *Joint first authors

Correspondance to:

Mr. J.A.G. Gibson, Institue of Life Sciences 2, Swansea University, Singleton Park,

Swansea, SA2 8PP, Email: j.a.g.gibson@swansea.ac.uk

Declarations of interest: None

Keywords :

Anxiety, Depression, Facial Scarring, Facial Trauma ;Prevalence

Abstract

Background: Facial scarring can have a dramatic effect on a patient's psychological health and wellbeing and present unique management challenges. This patient population remains poorly characterised in the contemporary literature.

Aims: To evaluate the prevalence of, and risk factors associated with affective disorders in adult patients with facial scars.

Methods: A systematic review was conducted using a protocol registered with PROSPERO and in line with the PRISMA statement. A comprehensive search of the literature was conducted using PubMed, MEDLINE, EMBASE, PSYCHInfo and The Cochrane Library.

Results: Twenty one studies were included, with a total of 2,394 participants. Using a random effects model, the weighted pooled prevalence of anxiety was 26.1% (95% CI 17.9%-36.3%) and the weighted pooled prevalence of depression was 21.4% (95% CI 15.4%-29.0%). Studies identified female gender, past psychiatric history and violent causation as factors associated with anxiety and depression.

Limitations: Included studies were limited to those published in peer reviewed journals. Longitudinal trends in both anxiety and depression were limited by a short duration of follow up.

Conclusions: There is a high and persistent burden of affective disorders in patients with facial scars. Additional research is required to further characterise this population and develop effective management strategies.

Introduction

It is estimated that 569,000 people are living with a facial disfigurement in the United Kingdom(Changing Faces, 2017). Aetiology for facial scarring is diverse and can be present at birth or acquired throughout life across all patient demographics(Bayat et al., 2003). In addition to physical symptoms, facial scarring can have significant psychosocial implications on a patient's health and well-being(Rumsey and Harcourt, 2004). Despite an improved understanding of scar pathophysiology and advances in surgical technique, effective treatment of facial disfigurement remains limited(De Sousa, 2008). It is, therefore, essential that the psychosocial needs of these patients are adequately assessed and addressed(Roberts and Gierasch, 2013).

The face is essential for social interaction and is thought to be the most important physical feature in formulating our perception of identity(Shaw, 1981). In a society which is pre-occupied with appearance and the pursuit of a "perfect" body image, the consequences of facial scarring can be far reaching.

Price (1990) developed one of the most recognised models of body image; consisting of three main components: body reality (the way our body actually is), body ideal (our perception of how our body should look, feel and behave) and body presentation (how our body appears to others). These components are influenced by individual coping strategies and social support networks(Price, 1990). The association of facial scarring and an altered body image is well documented in the literature(Macgregor, 1982, 1990; Rumsey and Harcourt, 2004). Facial scarring often leads to a pre-occupation with appearance, lower self confidence and negative perceptions from others; leading to an altered body image(Rumsey et al., 1986; Rumsey and Harcourt, 2004). This, in turn, creates a vulnerability to developing mental health conditions

(Rumsey and Harcourt, 2004). As demonstrated in numerous studies, facial scarring reduces health-related quality of life(Levine et al., 2005; Stubbs et al., 2011). However, there are few studies investigating the association between facial scarring and anxiety or depression.

Anxiety is defined by pathological worry or dread, that undermines normal function, whereas depression is characterised by low mood and anhedonia(American Psychiatric Association, 2013). Left untreated, both diseases are common causes of disability with a broad impact on morbidity and mortality which are well documented in the literature(Fawcett, 1993). Symptoms of depression and anxiety are linked with increased health costs, influence patient compliance with health care, substance misuse, unemployment and poor results in education(McLaughlin, 2011). This aspect of facial scarring is often overlooked by services that are primarily concerned with physical health, leading to sub-optimal care(Bisson et al., 1997). This occurs despite numerous authoritative publications prioritise psychological rehabilitation as one of their key recommendations following facial burns or trauma(Choudhury-Peters and Dain, 2016; National Network for Burn Care, 2013).

To our knowledge, the prevalence of anxiety and depression in patients with facial has not been systemically assessed. Therefore, a systematic review and meta-analysis was performed to assess the relationship between facial scarring and anxiety and/or depression. Given the extensive research into the psychosocial repurcussions of facial scarring, as outlined above, we hypothesised that the prevelance of anxiety and depression would be higher in this population group.

Methods:

Search Strategy and Selection Criteria

A systematic review protocol was developed in accordance with the Preferred Reporting for Items for Systematic Reviews and Meta-Analyses-Protocols (PRISMA-P) and registered with PROSPERO (CRD42017075415). The search strategy was constructed in line with PRISMA guidelines(Moher et al., 2009), the Cochrane handbook(Higgins JPT, 2011), and guidance from Terwee et al(Terwee et al., 2012). To identify all papers that investigated the association of facial scarring and anxiety and/or depression, three separate constructs were explored; Facial scarring, depression and anxiety. Searches were performed in MEDLINE (Ovid), Embase (Ovid), PyschINFO (Ovid), Cochrane and CINAHL (EBSCO). An example search strategy can be seen in *Supplementary Figure 1*. Grey literature and reference lists were also searched using Google and Google Scholar. Searches were performed by two independent researchers on the same day in September 2017, with results uploaded to the reference management software package, EndNote® Version X7 (Clarivate Analytics). Duplicates were removed using the functionality in EndNote®, with all references transferred to the online programme Covidence (www.covidence.org) for title and abstract screening. References were screened by two independent reviewers (EA and JG) according to the inclusion and exclusion criteria (Table 1), with all remaining articles downloaded in full-text format and re-screened. Discrepancies were discussed between the two reviewers with a third reviewer (TD) consulted if required.

Table 1. Inclusion and exclusion criteria for choosing studies.

Inclusion Criteria	Exclusion Criteria

• Any paper describing a study looking at facial scarring and depression or anxiety. • Any cause for facial scarring. • Any scoring system for depression or anxiety. • English language studies only.	• Non-English language papers. • Studies not investigating an association between facial scarring and anxiety or depression.

Data extraction and analysis

Data was extracted from all papers included in the final review by two reviewers (EA and JG). Data pertaining to study and participant characteristics, symptoms of anxiety and/or depression and method of measurement were extracted. All data were then uploaded to Excel (2016, Microsoft Corp., Redmond, USA) for analysis.

Assessment of Bias

Individual studies were assessed for risk of bias using the validated Quality in Prognosis Studies (QUIPs) tool (Hayden et al., 2013). Studies were assessed for bias in one of five domains; study participation, study attrition, outcome measurement, study confounding and statistical analysis and reporting. Each of the five domains was rated as having a high, moderate or low risk of bias. A summated score of the five domains was then calculated. Publication bias was assessed with funnel plots and Eggers test(Sterne and Egger, 2001).

Statistical Analysis

Between study heterogeneity was calculated using the I^2 statistic, a description of the percentage of total variation across studies caused by heterogeneity. A value of 0% represents minimal heterogeneity and higher values represent greater heterogeneity. Pooled data that

was classified as having low heterogeneity (I^2 <50%) were analysed using a fixed effects model, which assumes that studies are conducted under similar conditions (e.g same sample size, similar subjects). Pooled data that was classified as having moderate to high heterogeneity (I^2 >50%) were analysed using a random effects model, which adjusts for within and between study variability(Borenstein et al., 2010; Higgins et al., 2003).

Pooled prevalence was calculated based on dichotomous event rates and weighted based on sample size with a 95% CI. For longitudinal studies measuring prevalence at multiple time points, the prevalence at the final assessment was used for the pooled prevelance. Forest plots were generated to graphically display the results of the pooled analysis using DistillerSR Forest Plot Generator from Evidence Partners (Ottawa, Ontario, Canada). All statistical analysis was performed using the Comprehensive Meta-Analysis software package (Biostat, Englewood, New Jersey, USA).

Results

A total of 964 studies were identified using our search strategy, which after review left 21 articles conducted between 1996 and 2016, in our analysis (Table 2)(Bisson et al., 1997; Choudhury-Peters and Dain, 2016; Fares et al., 2014; Gandjalikhan-Nassab et al., 2016; Gironda et al., 2009; Hoogewerf et al., 2014; Hull et al., 2003; Islam et al., 2012a; Lento et al., 2004; Levine et al., 2005; Murphy et al., 2010; Prashanth et al., 2015; Rahtz et al., 2018; Robinson et al., 1996; Sen et al., 2001; Shetty et al., 2003; Shiraz et al., 2014; Tebble et al., 2006; Ukpong et al., 2007; Ukpong et al., 2008). Fifteen studies examined the prevalence of depression (Bisson et al., 1997; Choudhury-Peters and Dain, 2016; Fares et al., 2014; Gandjalikhan-Nassab et al., 2016; Gironda et al., 2009; Hoogewerf et al., 2014; Hull et al., 2003; Islam et al., 2012a; Rahtz et al., 2018; Sen et al., 2001; Shepherd et al., 1990; Shetty et

al., 2003; Shiraz et al., 2014; Ukpong et al., 2008; Versnel et al., 2012) and 13 articles examined the prevalence of anxiety (Bisson et al., 1997; Choudhury-Peters and Dain, 2016; Fares et al., 2014; Gandjalikhan-Nassab et al., 2016; Hull et al., 2003; Islam et al., 2012a; Rahtz et al., 2018; Sen et al., 2001; Shepherd et al., 1990; Shetty et al., 2003; Shiraz et al., 2014; Ukpong et al., 2008; Versnel et al., 2012); 13 articles looked at the prevalence of both anxiety and depression (Bisson et al., 1997; Choudhury-Peters and Dain, 2016; Fares et al., 2014; Gandjalikhan-Nassab et al., 2016; Hull et al., 2003; Islam et al., 2012a; Rahtz et al., 2018; Sen et al., 2001; Shepherd et al., 1990; Shetty et al., 2003; Shiraz et al., 2014; Ukpong et al., 2008; Versnel et al., 2012). Nine articles looked at mean depression scores and 7 articles looked at mean anxiety scores; 8 articles looked at both mean depression and mean anxiety scores. Studies were most commonly of cohort design (40%) and all studies were carried out in an outpatient environment. Nine of the studies (43%) were cross-sectional, without a second time-point, and 13 (57%) were longitudinal.
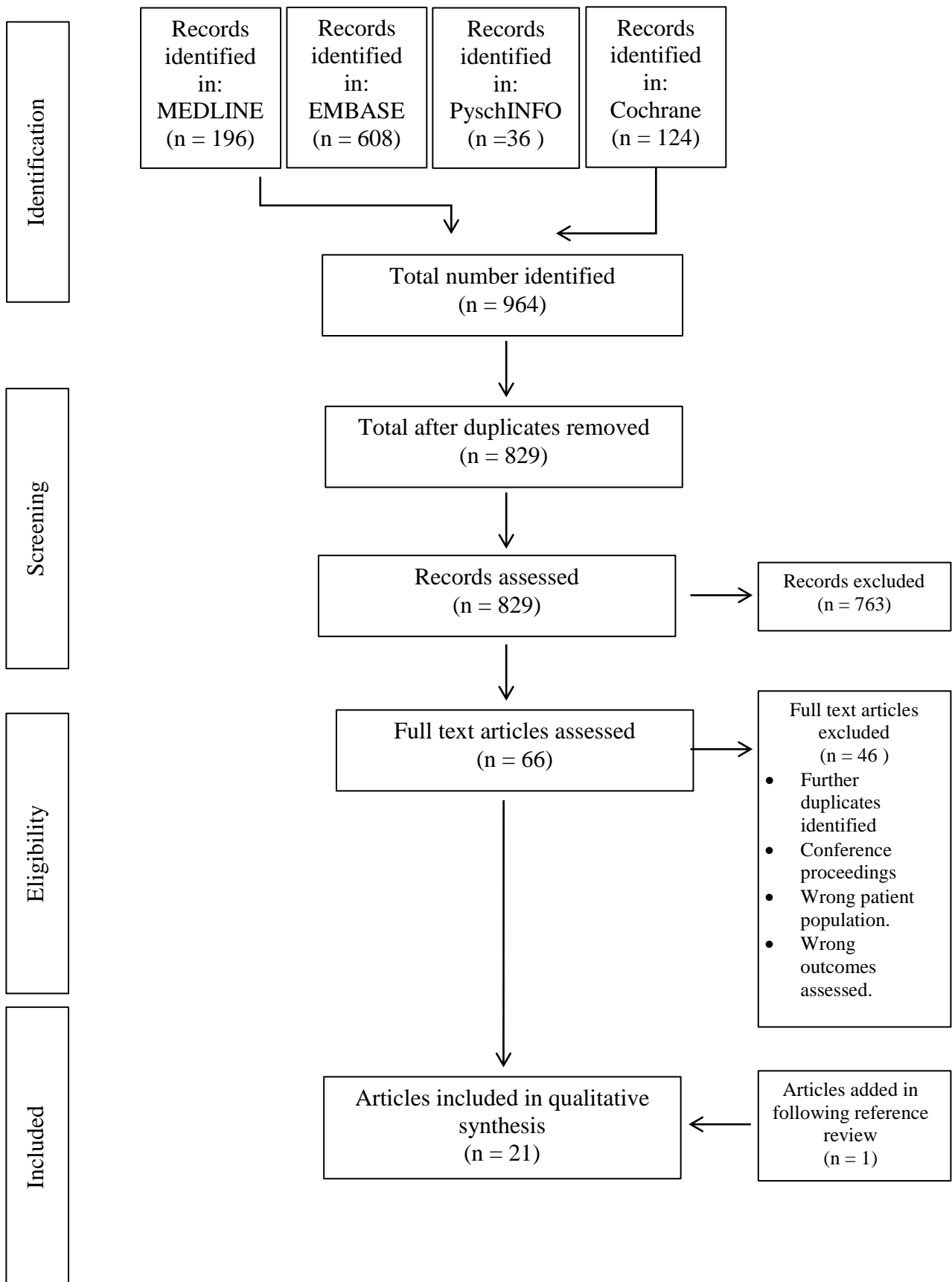
Figure 1 Prisma Flow Diagram.

Table 2: Summary of studies included and their characteristics

First Author	Year	Country	Study Design	Setting	Initial Sample Size	Time Since Scar-Event	Male (%)	Mean Age	Violent Cause	Depression	Anxiety
Bisson(Bisson et al., 1997)	1997	UK	Prospective Case Series	OPD	43	On Admission, 7 weeks	85	31	27	HADS	HADS
Choudhury-Peters (Choudhury-Peters and Dain, 2016)	2016	UK	Prospective Case Series	OPD	150	1-3 months, 6-9 months	73	NS	NS	Bespoke Questionnaire	Bespoke Questionnaire
Fares (Fares et al., 2014)	2014	Lebanon	Retrospective Case Series	Patient Records	29	Not specified.	76	27 (median)	100	DSM-IV	DSM-IV
Gandjalikhan-Nassab(Gandjalikhan-Nassab et al., 2016)	2016	Iran	Prospective Case-Control	IPD	50	Not specified.	60	21.3	NS	HADS	HADS
Gironda (Gironda et al., 2009)	2009	USA	Cohort	IPD, OPD	84	On admission, 1 month, 2 months, 3 months	87	35	NS	CES-D	NI
Hoogewerf(Hoogewerf et al., 2014)	2014	Netherlands	Prospective Case Series	OPD	132	3 weeks, 3 months, 6 months	83	40.2	NS	HADS	HADS
Hull (Hull et al., 2003)	2003	UK	Prospective Case Series	IPD, OPD	39	<10 days, 4-6 weeks	85	31	74	HADS	HADS
Islam (Islam et al., 2012a)	2012	UK + Australia	Prospective Case-Control	OPD	102	Cross-Sectional @ 3.5 weeks (mean)	77	33	NS	HADS	HADS
Lento (Lento et al., 2004)	2004	USA	Cohort	IPD, OPD	203	10 days, 6 months, 12 months	75	32	NS	BSI	BSI
Levine (Levine et al., 2005)	2005	USA	Retrospective Case Series	Patient Records	20	Cross-sectional @ 1 year 7 months (mean)	65	28	NS	CES-D	NI

Murphy(Murphy et al., 2010)	2010	USA	Retrospective Case-Control	OPD	71	Cross-Sectional @ <1 year	86	18	41	BSI	BSI
Prashanth (Prashanth et al., 2015)	2016	India	Cohort	IPD, OPD	153	Discharge, 1 month PO, 6 months PO	53	?	NS	HADS	HADS
Rahtz(Rahtz et al., 2018)	2018	UK	Cohort	IPD, OPD	107	21 days, 8 months	75	?	NS	HADS	HADS
Robinson (Robinson et al., 1996)	1996	UK	Cohort	Charity Workshop	64	Cross-Sectional @ 16.1 years	36	32.9	NS	HADS	HADS
Sen (Sen et al., 2001)	2001	UK	Prospective Case-Series	IPD, OPD	46	Pre-op, 12 months	91	34	NS	HADS	HADS
Shepherd(Shepherd et al., 1990)	1990	UK	Prospective Case-Series	OPD	70	1 week, 3 months	75	26	100	HADS, BSI	HADS, BSI
Shetty (Shetty et al., 2003)	2014	USA	Prospective Case Series	IPD, OPD	336	<10 days, 1 month, 6 months, 12 months	89	71% <40	83	BSI	BSI
Shiraz (Shiraz et al., 2014)	2014	UK	Prospective Case-Control	OPD	96	Not specified.	87	34	NS	HADS	HADS
Tebble (Tebble et al., 2006)	2006	UK	Prospective Case-Series	OPD	63	1 week, 6 months	81	30	NS	NI	STAI
Ukpong (Ukpong et al., 2008)	2008	Nigeria	Prospective Case-Series	IPD, OPD	126	<1 week, 6-8 weeks, 10-12 weeks	89	34	6	HADS	HADS
Versnel (Versnel et al., 2012)	2012	Netherlands	Retrospective Case-Series	Patient Records	59	Cross-Sectional @ 7-years	41	43	Excluded	HADS	HADS

OPD-Outpatient IPD-Inpatient NS – Not Specified HADS-Hospital Anxiety and Depression Score BSI- Brief Symptom Inventory CES-D – Center for Epidemiologic Studies Depression Scale
DSM-IV – Diagnostic Statistical Manual of Mental Disorders 4th ed NI- Not Included STAI- State Trait Anxiety Inventory

A total of 2043 patients were included in the 21 studies, 76% were male. Of the 18 studies that provided mean age data (n=1622), the mean age was 33 years. Eight studies (40%) looked at patients whose facial scars had a violent aetiology, two studies (10%) exclusively focused on this.

Fourteen studies (67%) used the Hospital Anxiety and Depression Scale to assess depression and anxiety. A non-objective measures of depression and anxiety was used in one study [23] and one study used a non-validated questionnaire [15].
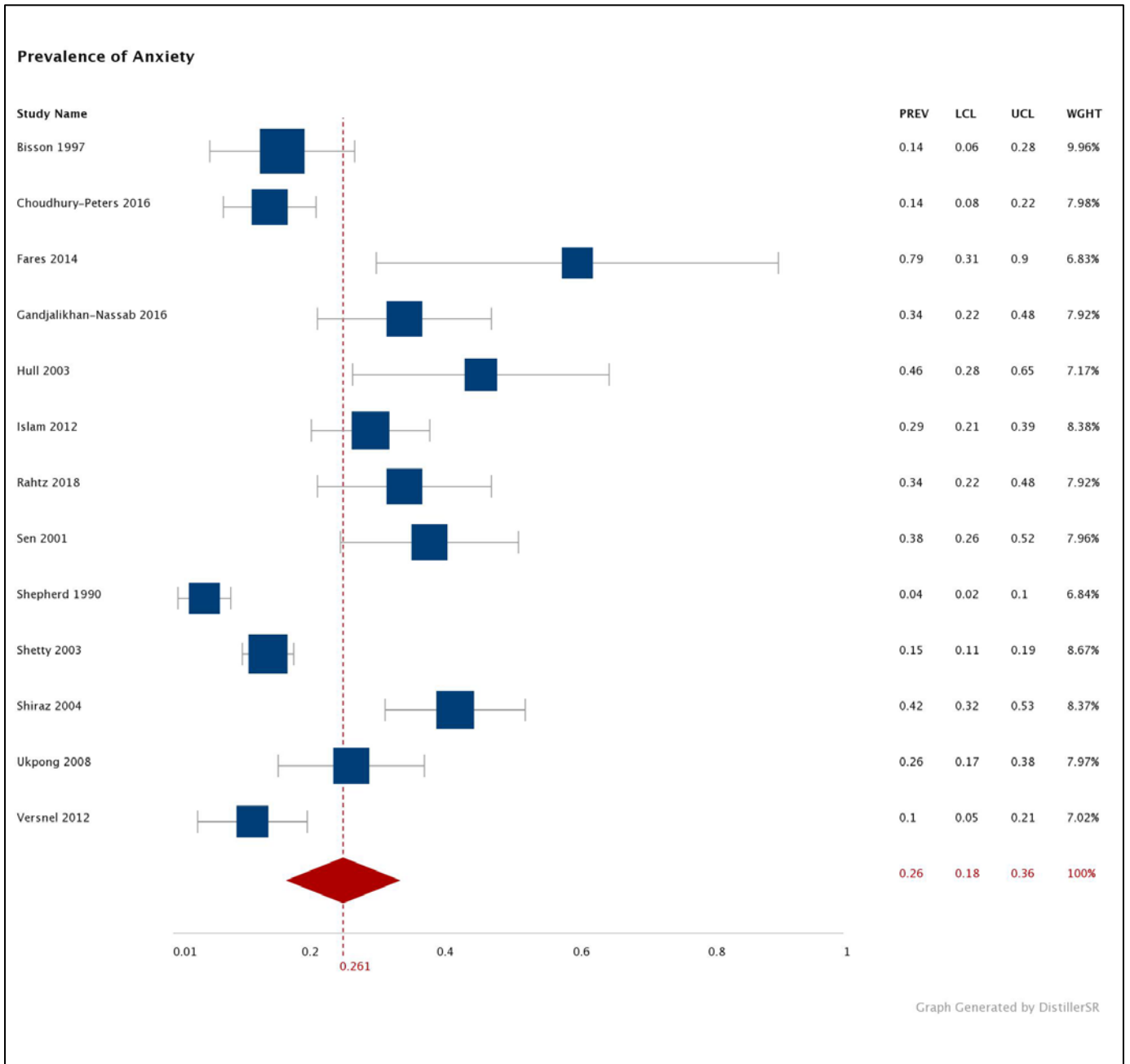
Prevalence

Between study heterogeneity was high in both studies that focused on anxiety (I^2=89.154) and depression (I^2=86.093).The weighted pooled prevalence, calculated using the random effects model is displayed in Table 3. Forest plots for the outcomes are displayed in Figure 2 (Anxiety) and Figure 3 (Depression). Sub group data were not presented in the majority of studies, thus subgroup analyses were not performed.

The highest prevalence of anxiety and depression was observed by Fares (Fares et al., 2014). In a small population of trauma victims 79.3% met the diagnostic criteria for anxiety and 72.4% met the criteria for depression. The lowest prevalence of anxiety and depression was reported by Versnel (Versnel et al., 2012) in a population with congenital facial deformities. Prevalence of anxiety was 11% and depression 5%.

Table 3 – Weighted pooled prevalence of anxiety and depression in patients following facial scarring using a random effects model.

|	Studies Included	N	Prevalence, %	95% CI
Anxiety	13	1113	26.1	17.9-36.3
Depression	15	1302	21.4	15.4-29.0

Figure 2 Forest Plot and pooled and pooled analysis of Anxiety Prevalence in Patients with facial scarring.

PREV –Prevalence LCL- Lower Confidence Limit UCL – Upper Confidence Level

WGHT-Weight

Figure 3 Forest Plot and pooled and pooled analysis of Depression Prevalence in Patients with facial scarring.
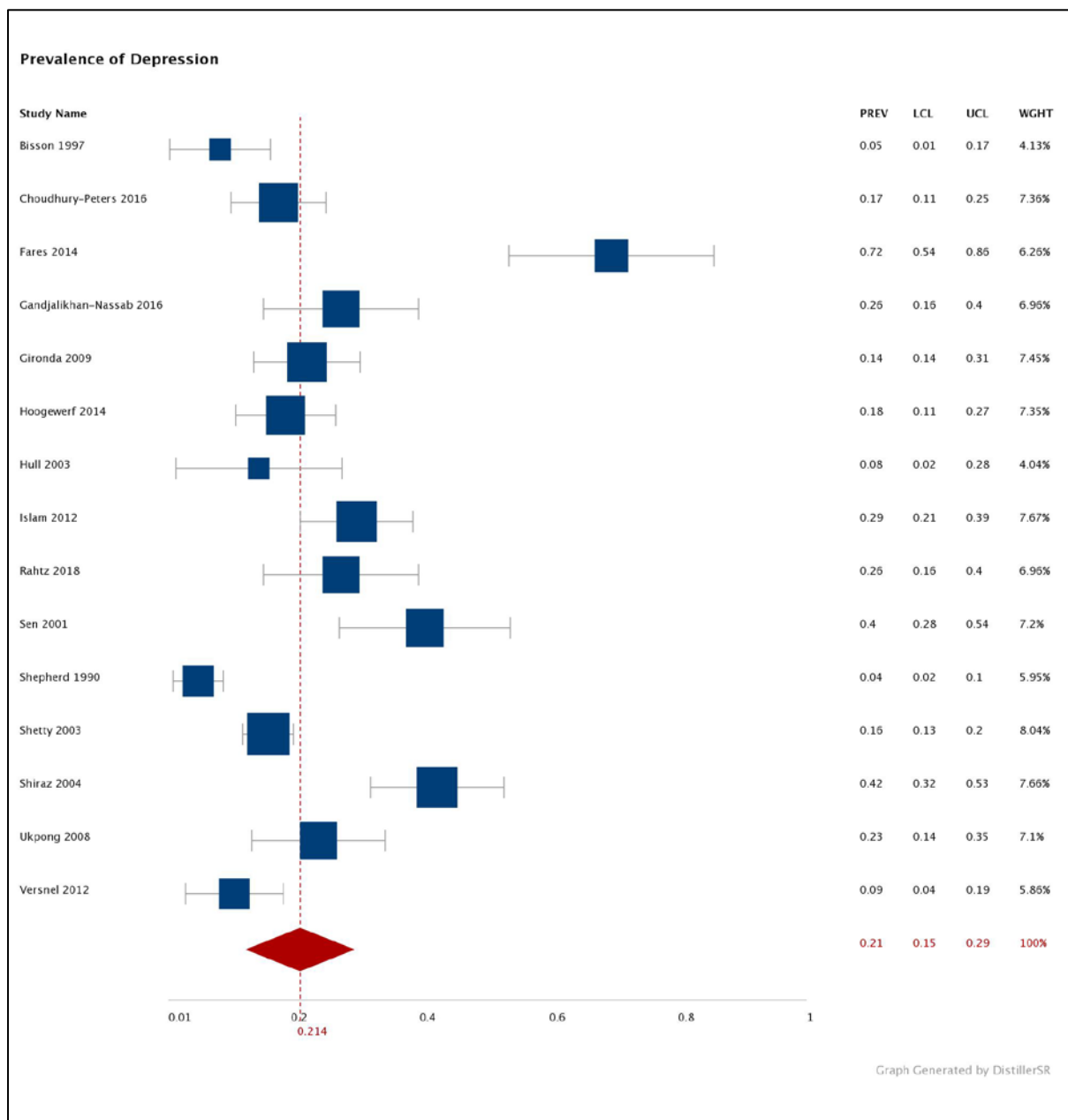
PREV –Prevalence LCL- Lower Confidence Limit UCL – Upper Confidence Level WGHT-Weight

Longitudinal Trends in Prevelance

The prevalence of anxiety decreased in six studies and remained static in two. The mean anxiety score decreased in all of the four studies that calculated mean anxiety scores at more than one time point. Depression followed a similar trend; prevalence decreased in eight studies and remained level in one. Of the studies that calculated mean scores over time, depression scores also decreased. The maximum follow up time was one year (Sen et al., 2001) whilst the minimum was seven weeks(Bisson et al., 1997). Pooled prevalence is displayed in Table 4 and Table 5.

Table 4- Pooled Prevalence of Anxiety Using a Random Effects Model

	Studies Included	N	Prevalence, %	95% CI
Time point 1 (7 days to 3 months post scarring)	8	73 4	24.4	13.4-40.0
Time point 2 (7 weeks to 1 year post scarring)	8	45 2	21.8	12.6-34.9

Table 5- Pooled Prevalence of Depression Using a Random Effects Model

	Studies Included	N	Prevalence, %	95% CI
Timepoint 1 (7 days to 3 months post scarring)	9	84 9	23.6	16.1-33.3
Timepoint 2 (7 weeks to 1 year post scarring)	9	54 7	16.1	9.8-23.3

Associated Factors

Of the 21 papers included in the review, eight considered factors associated with depression and anxiety. Being a victim of assault increased the prevalence of both anxiety and depression in a number of studies, compared to those that sustained a scar from an accident

(Bisson et al., 1997; Islam et al., 2012a; Murphy et al., 2010; Shepherd et al., 1990; Tebble et al., 2006). Conflicting evidence is present concerning scar severity; Tebble et al(Tebble et al., 2006) concluded that the size of scar was associated with increased depression and anxiety in patients with lacerations, however this observation was not noted in a population of patients with facial burns(Hoogewerf et al., 2014) where scar severity was not associated with depression or anxiety. The discrepancy could be explained by the differences in the mechanism of facial injury, the method of classifying scar severity or the degree of psychological trumatisation associated with different events. Tebble et al(Tebble et al., 2006) gained objective evidence by measuring scar length whereas patient rated scar severity was assessed by Hoogewerf(Hoogewerf et al., 2014).

Female patients were found to have an increased risk of anxiety(Gandjalikhan-Nassab et al., 2016; Islam et al., 2012b; Tebble et al., 2006) however this trend was not observed with depression(Hoogewerf et al., 2014; Shiraz et al., 2014). History of previous psychiatric disorder(Bisson et al., 1997) was associated with increased risk of depression whilst age and social support had no relationship with either depression or anxiety(Hoogewerf et al., 2014; Shiraz et al., 2014; Tebble et al., 2006).

Bias

Significant bias was noted amongst the studies; 17 studies were classified as having moderate or high risk of bias (Table 6). Frequently the study data did not reflect the study sample; patients lost to follow up were frequently not accounted for and reasons for study withdrawal were not often explored. Whilst the majority of studies incorporated a validated screening tool for anxiety and depression, the reporting of results was not entirely consistent. Several studies simply reported the mean score for the study population, omitting the proportion of

patients that had scores consistent with a diagnosis of anxiety or depression. This limits the clinical relevance of these studies. Asymmetry is noted in the funnel plots, however Eggers test was not significant for either anxiety (p= 0.13) or depression (p=0.31) indicating that publication bias was not present. Asymmetry of the funnel plots could be explained by the degree of heterogeneity between studies (Sterne and Egger, 2001).

Table 6- Assessment of bias

First Author	Year	Study Participation	Study attrition	Outcome Measure	Study Confounding	Statistical Analysis and Reporting	Overall
Bisson[12]	1997	High	High	Low	Low	Low	Moderate
Choudhury-Peters [15]	2016	High	High	Moderate	Low	Low	Moderate
Fares [23]	2014	High	N/A	Moderate	High	Moderate	High
Gandjalikhan-Nassab[24]	2016	High	N/A	Moderate	Low	Low	Moderate
Gironda [25]	2009	Moderate	Low	Moderate	Low	Low	Low
Hoogewerf[26]	2014	Low	High	Low	Low	Low	Low
Hull [27]	2003	Low	High	Low	Low	Low	Moderate
Islam [28]	2012	Low	Low	Low	High	Low	Low
Lento [29]	2004	Low	High	High	Moderate	High	Moderate
Levine [13]	2005	High	High	High	Low	High	High
Murphy[30]	2010	Low	High	High	High	High	High
Prashanth (Prashanth et al., 2015)	2016	Low	Low	Low	Low	High	Moderate
Rahtz (Rahtz et al., 2018)	2018	Low	moderate	Low	Low	low	Low
Robinson [32]	1996	Moderate	Low	Moderate	Low	Low	Moderate
Sen [33]	2001	High	High	Low	High	Low	Moderate
Shepherd (Shepherd et al., 1990)	1990	High	High	Low	High	High	High
Shetty (Shetty et al., 2003)	2014	High	High	Low	High	High	High
Shiraz (Shiraz et al., 2014)	2014	Moderate	Moderate	Moderate	Low	Low	Moderate
Tebble (Tebble et al., 2006)	2006	Moderate	Moderate	High	Low	High	Moderate
Ukpong (Ukpong et al., 2008)	2008	Moderate	Moderate	Low	High	Low	Moderate
Versnel (Versnel et al., 2012)	2012	Low	Moderate	Moderate	Low	High	Moderate

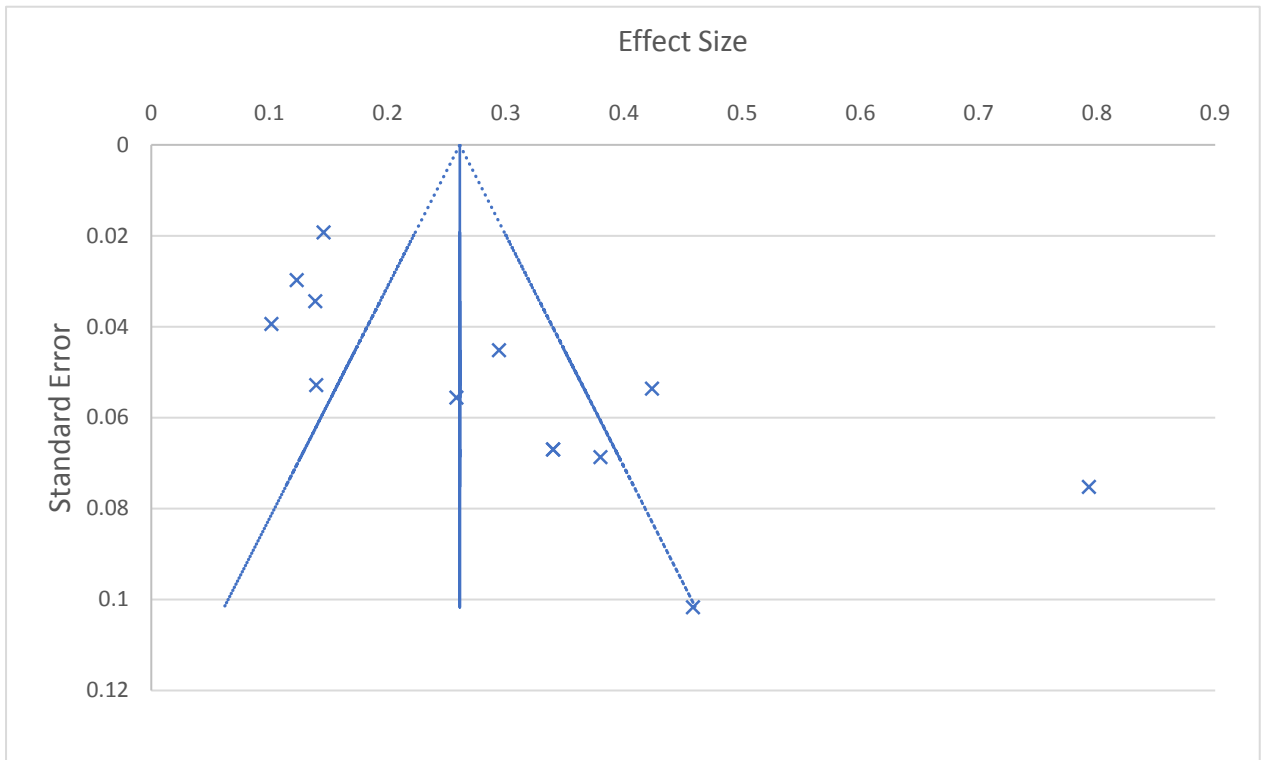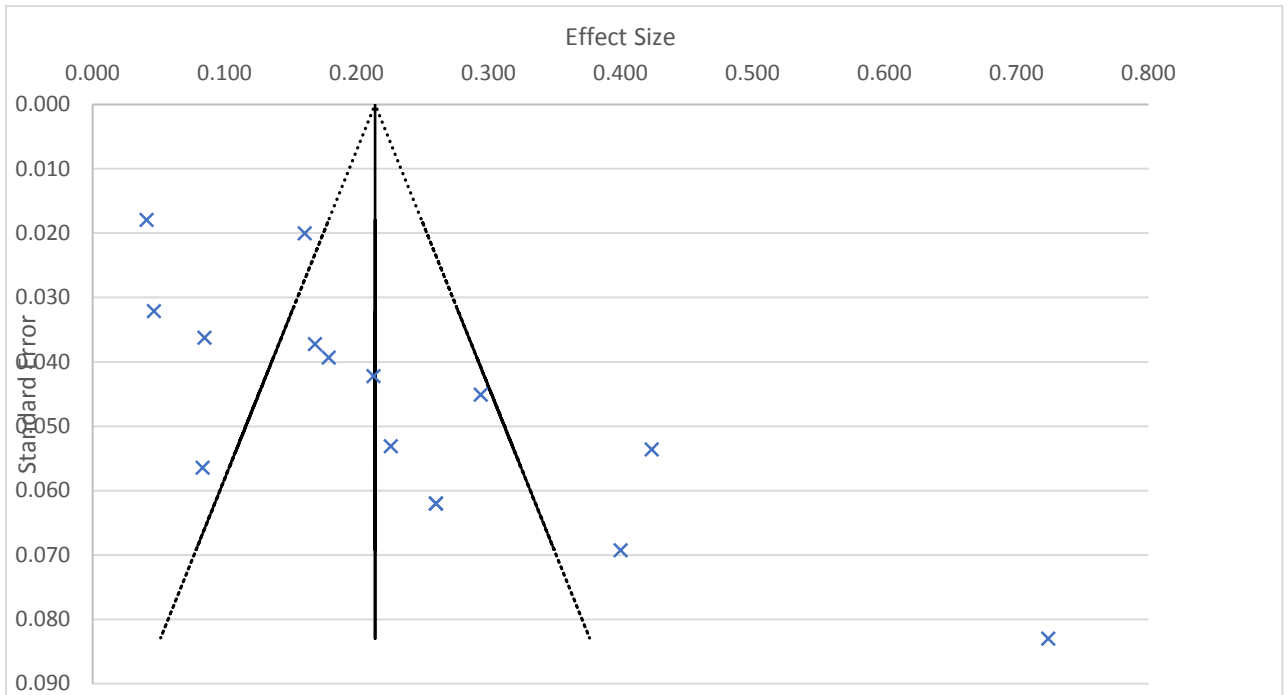**Figure 4 Funnel Plot of Prevalence of Anxiety**

Figure 5 – Funnel Plot of Prevalence of Depression

Discussion

This systematic review identified 21 studies examining the association of affective disorders and facial scarring. The prevalence of anxiety was 26% in patients with facial scarring whilst the prevalence of depression was 21%. The prevalence of anxiety and depression appear to decrease with time. The paucity of longitudinal data over one year, however, impedes our ability to fully characterise the trend in prevalence over time. Female gender, violent aetiology and premorbid psychopathology were identified as risk factors for anxiety and depression.

This review demonstrates that there is a significant burden of both anxiety and depression in patients with facial scarring, with both conditions being over-represented when compared to the general population, where the prevalence of anxiety disorders is 10.6% (Remes et al., 2016) and that of depressive symptoms 11.4%(Crawford et al., 2001). Explanations for these results are numerous. Rumsey and Harcourt (Rumsey and Harcourt, 2004) argue that the difficulties most commonly expressed by those with disfiguring conditions relate to a negative body image and difficulties with social interaction. In a study of young adults with cleft palates, 73% of participants reported low self confidence and unfavourable body image(Turner et al., 1997). These problems in turn lead to maladaptive thought processes (e.g fear of negative social evaluation) and negative behavioural patterns such as social avoidance. Social interactions are affected by visible differences in many ways. Making new friends can be difficult and reports of bullying are common(Turner et al., 1997). This is further compounded by the fact that many facial disfigurements may interfere with body language(Macgregor, 1990). These explanations are clearly simplistic and the weight of evidence suggests that the association is multifactorial.

The prevalence of mental illness is modulated by multiple factors. Several papers in this review demonstrated female gender to be associated with higher rates of psychopathology [18, 23, 24], a finding that is in keeping with general population studies (Bottomley et al., 2010; Merikangas et al., 2011). Other work has shown that females score higher on measures of maladaptation to disfigurement than males (Rahtz et al., 2018). Therefore, it may be that there is a composite relationship of female gender and facial scarring in the risk for developing psychopathology. Prevalence is also increased in patients who have scar(s) caused by violent methods[10, 18-21]; this is true of trauma patients in general(Rahtz et al., 2017). Finally, pre-morbid psychiatric illness was also shown to be associated with psychopathology[10] but this, unlike gender, was not controlled for in many of the case-control studies. This limits conclusions that can be drawn about the importance of previous anxiety or depressive episodes on the impact of facial scarring but it seems likely they are important given work in other populations (Bottomley et al., 2010).

Given methodological differences, it is difficult to directly compare our findings with other studies but the prevalence of anxiety and depression found in this study is slightly less than those reported for facial palsy(Fu et al., 2011) and facial paralysis(Pouwels et al., 2016). The findings suggest that facial scarring may result in a similar burden of depression but lower burden of anxiety than seen in acne patients(Lukaviciute et al., 2017), and a lower burden of depression compared to orthopaedic trauma patients(Muscatelli et al., 2016). When compared to patients with chronic medical disorders, however, there is a higher prevalence of depression with facial scarring patients compared to Diabetes Mellitus (9.3%), Chronic Obstructive Pulmonary Disease (COPD) (15.4%) and End-Stage Renal Disease (ESRD) (17.0%)(Egede, 2007). Patients with the latter conditions routinely receive more regular contact from health care providers and, therefore, there is greater opportunity to identify

developing psychological comorbidity. Whether this, the actual disfigurement or other factors underly the disparity in prevalence is unclear and either way there is an evident shortfall in psychological care for patients with facial scars.

Limitations

This systematic review and meta-analysis combined data across studies in order to estimate the prevalence of depression and anxiety in patients with facial scarring. The main limitation of this study, as with most reviews, is that patient populations, outcome measures and clinical settings are not homogenous across studies. Notably, there was great variation in the metrics used, timing of diagnostic screening and thresholds used to define depression and anxiety. Furthermore, the data presented in the studies limits our ability to comment on the severity of the depression or anxiety. The lack of longitudinal data bias the findings towards the initial phase of recovery and makes comparison of prevalence at different time points difficult. Whilst confounding factors were established in a few studies, there remains a paucity of information on risk factors for depression and anxiety in this group of patients. Finally, the design of the included studies was able to demonstrate associations but did not allow the inference of causality to be made.

Conclusions

Overall, there is a considerable burden of anxiety and depression in patients with facial scars. From a clinical perspective, our study has demonstrated the requirement for formal mental state assessment in trauma clinics; this being infrequently perfomed at present. Early detection and treatment are likely to improve the health and wellbeing of patients with facial scars who suffer from anxiety and depression. Factors such as gender, past psychiatric history and violent circumstances of facial injury are all associated with increased prevalence

and dissemination of this knowledge will help healthcare providers detect, treat and offer additional support to this select patient group.

The optimal strategy to holistically detect and treat anxiety and depression in facial scarring remains unkown. Future studies should aim to determine the efficacy of existing treatment options and consider the need for development of more bespoke approaches for this select patient group. Further work is also required to determine the longitudinal relationship of anxiety and depression in patients with facial scarring.

Supplementary Figure 1

Search strategy

#1 Facial Injury*.mp

#2 Facial Injuries MeSH term explode all trees

#3 Facial Trauma .mp

#4 Facial Scar*

#5 Facial Scarring

#6 Anxiety Disorder MeSH term explode all trees

#7 Anxiety .mp

#8 Depression .mp

#9 Depression MeSH term explode all trees

#10 #1 OR #2 OR #3 OR #4 OR#5

#11 #6 OR #7 OR #8 OR #9

#12 #10 AND#11

(facial injuries.mp. OR exp facial injuries/ OR facial trauma.mp. OR facial burn.mp. OR facial scar.mp OR facial scarring.mp.) AND (exp anxiety disorders/ OR anxiety.mp. OR exp anxiety/ OR depression.mp. OR exp depression/)

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	4
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	4
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	5
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	4,5
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Supplementary figure 1
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	4,5
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	6
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	6

Section/topic	#	Checklist item	Reported on page #
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	6
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	6
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	6

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	6
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	N/A
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	8
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	9
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	15
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	12,13
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	11-14
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	15,16
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	N/A
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	17
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	18

Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	19
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	19

For more information, visit: **www.prisma-statement.org**.

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