



Efficacy of group CBT Vs group information and support in relapse and recurrence of depression in adults

Kelly, A., & Cassidy, T. (2016). Efficacy of group CBT Vs group information and support in relapse and recurrence of depression in adults. *Journal of Psychology and Clinical Psychiatry*, 5(5).
<https://doi.org/10.15406/jpcpy.2016.05.00305>

[Link to publication record in Ulster University Research Portal](#)

Published in:
Journal of Psychology and Clinical Psychiatry

Publication Status:
Published (in print/issue): 07/04/2016

DOI:
[10.15406/jpcpy.2016.05.00305](https://doi.org/10.15406/jpcpy.2016.05.00305)

Document Version
Publisher's PDF, also known as Version of record

General rights

The copyright and moral rights to the output are retained by the output author(s), unless otherwise stated by the document licence.

Unless otherwise stated, users are permitted to download a copy of the output for personal study or non-commercial research and are permitted to freely distribute the URL of the output. They are not permitted to alter, reproduce, distribute or make any commercial use of the output without obtaining the permission of the author(s).

If the document is licenced under Creative Commons, the rights of users of the documents can be found at <https://creativecommons.org/share-your-work/licenses/>.

Take down policy

The Research Portal is Ulster University's institutional repository that provides access to Ulster's research outputs. Every effort has been made to ensure that content in the Research Portal does not infringe any person's rights, or applicable UK laws. If you discover content in the Research Portal that you believe breaches copyright or violates any law, please contact pure-support@ulster.ac.uk

Efficacy of Group CBT Vs Group Information and Support in Relapse and Recurrence of Depression in Adults

Research Article**Abstract**

This study aimed to analyse the rates and length of time to relapse and/or recurrence of depression in individuals who attended either Group CBT or Group Information and Support in an adult secondary mental health setting in Ireland. The present study centred on the analysis of previously collected data from groups running between 2005 and 2010 and on the retrospective file review. It formed part of a larger scale research study conducted by the Principal Clinical Psychologist evaluating the effectiveness of CBT for depression and bipolar disorder. The study was quantitative in nature and incorporated qualitative elements (i.e. Clients' and Practitioners' description of the severity of the depressive episodes) which were converted into quantifiable categories. Participants comprised of two groups: Treatment I (Group CBT) including participants who attended 8 or 12 sessions of manualised Group CBT and a comparison sample: Treatment II (Group Information and Support) comprised of participants who attended 12 sessions of group information and support. Based on survival analysis, no significant difference was found in effectiveness for Group CBT and Group Information and Support in preventing and/or decreasing the number and the length of time to relapse and/or recurrence of depression in this client group. Findings, clinical implications, methodological limitations and future research directions were also discussed.

Volume 5 Issue 5 - 2016

Aleksandra Kelly and Tony Cassidy **Department of Psychology, Ulster University, Northern Ireland*

***Corresponding author:** Tony Cassidy, Department of Psychology, Ulster University, Cromore Road Coleraine Northern Ireland BT52 1SA, Northern Ireland, Tel: +44(0)28 70123025; Email: t.cassidy@ulster.ac.uk

Aleksandra Kelly, Department of Psychology, Ulster University, Cromore Road Coleraine Northern Ireland BT52 1SA, Northern Ireland

Received: February 08, 2016 | **Published:** April 07, 2016**Introduction**

The World Health Organisation [1] has estimated that depression will reach the status of the second most significant cause of disability worldwide by year 2020. Depression is a common and serious mental health disorder. It is marked by symptoms such as sadness and depressed mood; loss of interest and pleasure; feelings of guilt or low self-worth; changes in appetite and sleep; and poor concentration [2]. The disorder leads to 'clinically significant distress' and a decline in functioning across social, occupational and personal areas of life. It is frequently accompanied by suicidal ideation, attempts, and completed suicides [2]. Review of a number of studies suggests that the prevalence rates vary cross-culturally and among different age, gender and other variables groups. Based on data from 14 European countries, WHO has estimated the gender prevalence of depressive episodes at 16 per 100,000 per year for males and 27 per 100,000 per year for females [3].

The emergence of longitudinal studies of depression marked a shift in the understanding of this disorder from an "episodic" to a "lifelong" condition [4]. The severity of the condition can vary. Depression ranges on a spectrum from mild, through moderate to severe and can present with or without psychotic features such as delusions or hallucinations experienced during the depressive episode [5]. The major depressive episode may be at the core of the diagnosis of major depressive disorder or may be considered part of other mood disorders including bipolar spectrum disorders and "double depression" i.e. major depressive

disorder and dysthymia [2]. Diagnostic criteria for dysthymia comprise chronically depressed mood lasting a minimum of two years, together with at least two other symptoms of depression described above. The symptom-free period in dysthymia does not exceed two continuous months in duration. Generally, dysthymia can be characterized by less severe symptoms compared to major depressive disorder [5].

The frequently chronic nature of depression places individuals at an increased risk of a long-term vulnerability. Keller [4] highlights the distinction in prognosis between individuals with first-time experience of depression and those with a past history of a minimum of three depressive episodes. It is estimated that those with a past history of at least three past depressive episodes are approximately three times more likely to relapse compared to the "first-timers". Additionally, research suggests that the sooner the relapse occurs following recovery, the higher the likelihood of the chronicity of depressions (estimated at 20%), based on data emerging from a five-year follow-up [4].

There is a more recent shift to use a minimum of two episodes as a reliable predictor of future re-occurrence of depression [4]. This has been reflected in the DSM-IV [2]. Depression frequently requires expensive and extensive treatment programmes due to the condition's recurrent nature [6]. It is often co-morbid with other mental and physical health issues and can either develop in response to and exacerbate the condition, or can leave the individual vulnerable to other disorders or illnesses. The bi-directional relationship between depression and physical health

has been of considerable interest to researchers, especially in areas such as chronic pain [7,8], chronic fatigue [9], cancer [10,11], coronary heart disease [12,13], HIV/AIDS [14,15], rheumatoid arthritis [16,17], and functional somatic syndrome [18] to name a few. These are costly health issues that entail long recovery processes. Co-morbid medical conditions have also been found to contribute to an increased risk for a relapse of depression [19].

Group approaches have been found to produce positive effects on depressed individuals, as group settings tend to facilitate mutual support and understanding [20]. Group treatments have grown in popularity among mental health practitioners due to their relative cost-effectiveness as well as their contribution to the waitlist reduction. In addition to support groups, a wide range of therapeutic groups have been established in the recent years, many of which are predominantly CBT- and/or mindfulness-based. Their long-term effectiveness, however, has not been extensively explored, with limited survival analyses currently available.

Yalom [21] identified nine essential therapeutic factors, that impact the change process, which the group experience can provide:

- a) Instillation of hope, universality (sense that the experienced problems are not unique)
- b) Imparting information (didactic instruction and direct advice)
- c) Altruism (helping other group members via giving advice or information; expressing empathy, understanding and support)
- d) The corrective capitulation of the primary family group and interpersonal learning (via the “social microcosm” that the group format provides and the feedback on and “correction” of the interpersonal patterns provided by facilitators and group members)
- e) Development of socializing techniques (implicitly or via direct practice)
- f) Imitative behavior (via vicarious or observational learning)
- g) Group cohesion (embedded in acceptance, support and trust)
- h) Catharsis (achieved via “unburdening”, verbalizing and self-awareness)

Psychotherapeutic approach to depression, in both individual and group format, has been examined and evaluated by a wide range of broad and meta-analytic reviews. Robinson reported almost identical treatment effect sizes (Cohen’s d) for individual therapy (.83; SD .77) and group therapy (.84; SD .60), based on an evaluation (and comparison to a wait-list control) of 15 studies using individual treatment and 16 using group treatment [5].

Meta-analysis of psycho educational approach to depression (review of Lewinsohn’s ‘Coping with Depression’ course) indicated similar effectiveness of CBT-based psycho education for unipolar depression when compared to other treatments [22]. Some sources indicate that the effectiveness of a group CBT is comparable to an individual CBT [23].

Despite some potential drawbacks (monopolisation, confrontation, formation of sub-groups, different pace of acquiring skills, varying severity of the condition, practical issues of attendance etc), group work has many advantages over individual approaches. Clients generally find it easier to identify the cognitive distortions and biased thinking of others and then apply the skill to their own cognitions, with group members frequently filling the role of co-therapists [24]. The group setting also provides an opportunity for modelling the desired behaviours by group facilitators and members by displaying empathy, support and encouragement, as well as promoting change via challenging negative automatic thoughts and distorted cognitions. These have been found useful in dealing with “depressogenic” group processes such as social comparison, refusal of help and assistance, as well as suicidal or self-harm ideation [5].

Cognitive behavioural therapy (CBT) is an evidence-based approach and one of the most researched psychosocial treatments for depression [2]. Its effectiveness has been supported by evidence from numerous randomised control trials, uncontrolled trials, case series, and case studies [25-27]. Extensive review of the rates of relapse and recurrence of depression following recovery in individuals who received either cognitive therapy (CT) or antidepressant medication (ADM) revealed that CT decreased the rates to 20-36% compared to 50-78% for ADM [4]. Support for these findings has consistently found in cross-cultural studies (with vast majority emerging from the UK and the USA), with various types of ADM, various CT practitioners, and different follow-up periods.

Extensive literature focuses on the links between depression and individuals’ maladaptive attitudes and cognitive biases [28]. The Beck’s et al. [29] model of depression is based on ‘depressive cognitive triad’- negative automatic thought patterns with regards to oneself (accompanied by guilt, blame, and self-criticism), the world (characterised by attending to the negative and anhedonia), and the future (pessimism and hopelessness) [29]. These dysfunctional cognitions are associated with negative emotions, maladaptive behaviours, and negative physical responses. Key components of CBT for depression encompass behavioural strategies (e.g. activity scheduling, goal setting); cognitive strategies (e.g. thought records and core belief work); and relapse prevention strategies [30].

Since CBT provides clients with tools to use post treatment, it is “likely to have more lasting and potentially prophylactic effect than comparator conditions such as antidepressant medications” [5].

Many individuals will experience multiple episodes of depression throughout their lives [31]. These are often, but not always, precipitated by a wide range of negative life events including losses, interpersonal difficulties, rejections and disappointments [4]. Although a wide range of treatments for depression are currently available, their effectiveness short and long-term can vary significantly.

Last decade has seen an increase of studies investigating the efficacy of the various therapy treatments. Findings are encouraging for mindfulness- based cognitive therapy (MBCT) as a cost-efficient intervention, effective in preventing relapse/recurrence of depression in recovered individuals [32]. These promising effects of MBCT were found only in participants who

had experienced three or more episodes of depression prior to treatment, indicating that the number of the episodes may be an important factor impacting the efficacy of the intervention. Based on survival analyses, Bockting et al. [33] indicated that cognitive therapy (CT) may be an effective treatment option for depressed individuals following a remission. This is particularly the case for those with five or more prior episodes of depression. CT was found to reduce relapse/recurrence rates from 72% to 46% in these individuals.

The efficacy of treatment can be evaluated in relation to response, remission, recovery, relapse, and recurrence, definitions of which vary substantially across different sources. Response refers to significant improvement or 'clinically relevant reduction (e.g. $\geq 50\%$) on a severity scale' such as BDI [34]. Remission occurs when only 'few signs of illness remain' [35] and individuals are 'asymptomatic' i.e. no longer meeting criteria for major depressive disorder [36]. Remission indicates presence of minimal residual symptoms of depression only. Some studies link residual symptoms with an increased probability of recurrence of depression [37-39], while other studies do not report such findings [40-42].

There is also lack of consensus whether the number of depressive episodes can be considered a predictor of recurrence of depression, with some studies providing support [37,43] and other studies reporting no such findings [41,44].

Despite lack of a standardised definition of recovery, it is often defined as 'a sustained period of remission' [34], while relapse is defined as an increase in symptoms occurring within 6 months after initial response to treatment [36]. Relapse indicates "the worsening of a previously controlled episode that had not yet run its course" rather than experiencing a new episode [4]. Recurrence refers to a new episode of depression following recovery [34] and commonly occurs 6 + months after the response to treatment or remission [36]. Data suggests that each depressive episode enhances the likelihood of early recurrence, with briefer time intervals observed between recurrences [4].

Meta-analytic reviews indicate that cognitive therapy (CT) is an effective treatment and a successful preventive intervention for depression [45-48]. Eight studies reported 29.5% recurrence rate for CT/CBT compared with 60% for antidepressant medication 1 year after treatment completion [45]. Behavioural activation has also been found to produce enduring effects comparable to CT [49]. Both CT and behavioural activation are considered to be long-lasting and cost-effective alternatives to pharmacological treatment [49].

For the purpose of this study, the focus was on a broader categorization of depression to include major depressive disorder, dysthymia and "double depression", whilst excluding major depressive disorder with psychotic features and bipolar spectrum disorders. The present study adds to existing research exploring relapse and recurrence of depression in adults attending a secondary adult mental health service. It also provides information about the efficacy of group CBT treatment and group information and support in preventing and/or decreasing relapses and recurrences of depression in this client group.

The study centred on the survival analysis- a statistical analysis of relapse and recurrence originally used to examine the effectiveness of treatment in prolonging life for people with terminal illnesses [2]. This has since been applied to depression to investigate the length of time an individual will remain symptom-free or with residual depressive symptoms before they become depressed again.

Methodology

Design

This study is quantitative in nature and comprised a retrospective review of data collected for all individuals who participated in treatment I and II between 2005 and 2010 (inclusive), as well as past and current client files. Qualitative elements such as clients' and practitioners' description of the severity of the depressive episode and care plan comments pertaining to relapse or recurrence of depression (i.e. medication increase/decrease, day hospital admission or additional psychological supports recommendations) were subsequently converted into quantifiable categories.

Participants

Participants were recruited from a larger project conducted through a secondary care, Community Adult Mental Health Service in Dublin, Ireland between 2005 and 2010. The initial sample comprised 244 participants. There were 68 participants included in the study. Full details of the selection, inclusion and exclusion criteria are provided below.

(i) Treatment I (Group CBT)

This sample includes participants who attended 8 or 12 sessions of manualised CBT group therapy group between 2005 and 2010 (N=43).

Comparison sample:

(ii) Treatment II (Group information and support)

This sample included participants who attended 12 sessions of group information and support between 2005 and 2010 (N=25).

(iii) Treatment inclusion/exclusion criteria

All treatment I and II participants were between 18 and 64 years old at the time of attending either group, met DSM-IV criteria for depression, represented both genders, and had sufficient literacy skills to complete the assessment protocol.

Treatment exclusion criteria included referred individuals who were unable to complete the assessment protocol due to literacy difficulties, or unable to attend the full course of the programme. Individuals presenting with a primary diagnosis of schizophrenia, an organic disorder, or current active substance abuse disorders were also excluded from the study. Additionally, those who were still inpatients or who had participated in another research project within the previous 4 months were also excluded.

Participants were not randomly assigned. After being assessed for the group, all individuals were wait-listed for the next available intervention (either CBT group therapy or Group Information and

Support).

Materials and Measures

Demographic/additional information

Demographic and additional information was obtained for all participants from existing files. Variables of interest included, gender, age, socio-economic status, history of depression (age at onset), physical health issues, medication (benzodiazepines, antidepressants, major tranquilisers, and other psychiatric medication at the start of group and at final follow up), prior suicide history, prior self-harm history, prior substance abuse history, prior psychiatric hospital; attendance history, prior day hospital attendance history, and prior exposure to psychological input history.

Measures/instruments

The following measures previously administered to participants were utilised:

Structured Clinical Interview for DSM-IV: Axis 1 Disorders, Clinician Version (SCID-CV), (SCID-I) (First, Spritzer, Gibbon & Williams, 1996)- a semi-structured interview administered by a Clinical Psychologist or trained Assistant Psychologist allowing for a consistent clinical diagnosis. The items on SCID-I reflect the diagnostic criteria for DSM-IV. SCID-I was used to categorise participants with regards to their primary diagnosis and co-morbid diagnosis. SCID-I reports good levels of internal consistency (Cronbach's alpha .80) and the test/retest reliability between .61 to .73.

Beck Depression Inventory-II (BDI-II): a 21-item self-report measure of the severity of depression widely used in psychiatrically diagnosed adults and adolescents aged 13 or older as well as non-clinical population. The instrument is composed of items relating to symptoms of depression (e.g. hopelessness and irritability), cognitions (e.g. pessimism and past failure), and feelings (e.g. guilt and sadness), as well as physical symptoms (e.g. fatigue and changes in sleeping pattern). Overall scores between 0-13 indicate minimal depression; scores between 14-19 correspond with mild depression; scores between 20-28 indicate moderate depression; and 29-63 suggest severe depression. The BDI-II is in line with the diagnostic criteria for depression outlined by DSM-IV. Each item is rated on a 4-point scale. Beck et al. [50] report high levels of internal consistency (Cronbach's alpha = .92) and test/retest reliability score of .93.

Beck Anxiety Inventory (BAI): a 21-item self-report measure of anxiety over the past week composed of items relating to symptoms of anxiety including physical symptoms, cognitions and emotions. This screening tool has been found to be highly sensitive to anxious and non-anxious individuals in a range of clinical populations. Each BAI item is rated on a 4-point scale ranging from 'not at all' to 'severely'. The BAI reports good levels of internal consistency (Cronbach's alpha scores between .92 and .94) and test/retest reliability (.75) [51].

Clinical Outcomes in Routine Evaluation (CORE): a 34-item self-report measure of outcome in adult mental health outpatients who received psychosocial interventions. The instrument is composed of four sub-scales: subjective well-being; symptoms;

functioning; and risk. Internal consistency (Cronbach's alpha) for the four subscales ranges from .75 to .94; the test-retest reliability has been found to range from .88 to .94 [52].

The World Health Organisation Quality of Life Brief Version (WHO-QoL-Bref): a 26- item self-report measure of quality of life. The instrument is composed of two 5-point scales ranging from 'not at all/very dissatisfied' to 'an extreme amount/very satisfied', in addition to scores on four dimensions including: physical health; functioning; social relationships; and the environment. Its internal consistency(Cronbach's alpha) ranges from .66 to .84, with the test/retest reliability from .66 to .87 [53].

Dysfunctional Attitudes Scale (DAS): a 40-item scale measuring the intensity of negative attitudes towards oneself, the outside world, and the future. Each item comprises of a negative statement and a 7-point scale ranging from 'fully agree' to 'fully disagree'. 10 items are reversely coded. It has been found to have a good internal consistency (Cronbach's alpha .90) and test-retest reliability of .73 [54].

Procedure

Treatment Procedure

All referrals were made by multi-disciplinary teams. A structured screening interview to assess the individual's suitability for group was carried out. Participants were requested to complete questionnaires (BDI-II, BAI, CORE, WHO-QoL-Bref, DAS, Life Events Scale, CBT Beliefs Scale, and URICA) and to read and discuss chapter 4 from Depression-The Common Sense Approach [55].

Exclusion criteria were as above (see 'Participants' in Methodology section).The remaining participants were assessed using SCID-I to establish their diagnostic status. All participants with BDI score of 14 (mild depression) or more were allocated to the next available treatment programme, either Group CBT (treatment I) or Group Information and Support (treatment II). Participants in treatment I and II were offered 8 or 12 two-and-a-half-hour sessions (including a 30-minute break) for Group CBT and 12 two-and-a-half-hour sessions (including a 30-minute break) for Group Information and Support. Sessions were held twice weekly for duration of 6 weeks, followed by 6 booster sessions held at monthly intervals in St. John of God Hospital in Still organ, Co. Dublin. These were closed groups. The treatment I sessions focused on psycho education, behavioural activation, dealing with negative thinking, and cognitive restructuring. Sessions included a check-in, review of homework, presentation of new material, group discussion and practicing of new skills, and finally setting homework. The treatment II sessions comprised of psycho education only. The monthly follow-up sessions centred on a review of the progress and revision of skill set use/mastery, with no new material introduced. All relevant questionnaires were completed at pre-treatment (time 1), post-treatment (time 2), and final follow-up session (time 3). Additionally, BDI-II and BAI were completed at each session.

The Group CBT and the Information and Support group manuals were developed by the Principal Clinical Psychologist. Session delivery was evaluated by and external, CBT trained Clinical Psychologist, using the Cognitive Therapy Scale (Young & Beck, 1980). All sessions for both groups were facilitated by

the Principal Clinical Psychologist and/or a Senior Counselling Psychologist. Assessments were conducted by trained Assistant Psychologists, under the supervision of the Principal Clinical Psychologist.

Analysis procedure

All analyses were conducted on participants who attended at least 6 out of 8 group sessions (8-session group) or 9 out of 12 group sessions (12-session groups) and 3 out of 6 group follow-up sessions (“completers”) with the primary diagnosis of depression. The samples were compared on their demographic and pre-treatment characteristics. Since the primary research question was whether either type of treatment is more effective at protecting against the subsequent relapse and/or recurrence of depression, both treatment conditions were pooled for the analyses.

No measures were administered to any of the participants. Treatment I and II participants previously completed all the self-report measures and a semi-structured interview (SCID) prior, during or post-treatment. All the quantitative data extracted from the self-report measures was managed using SPSS (Statistical Package for the Social Sciences version 19).

All relevant information pertaining to relapse and recurrence of depression, as well as demographic (gender; age; socio-economic status) and additional data (history of depression; physical health issues; medication; prior suicide, self-harm and substance abuse history; prior psychiatric and day hospital attendance history; prior exposure to psychological input) were extracted from the service’s computerised client database - the Mental Health Information System (MHIS) and hardcopy files. Access to files was granted on a strictly need-to-know-basis.

Relapse of the depressive episode was defined as a substantial increase in the BDI score at the six monthly follow-up group sessions, based on the BDI scores collected at each of the group. A substantial increase in score was indicated by a shift from a lower-level depression category to a higher-level category (i.e. from mild to moderate category or from moderate to severe category) which persisted for at least two sessions or for one session when accompanied by an augmentation or increase of antidepressant medication, suicide attempt, or acute day hospital referral.

An episode of recurrence of depression was established on the basis of the practitioners’ clinical assessments, as outlined in the client files, based on the following criteria:

- (a) an increase in dosage of antidepressant medication due to an increase in the severity of depressive symptoms
- (b) an augmentation of antidepressant medication due to an increase in the severity of depressive symptoms
- (c) a change of antidepressant medication if unresponsive to treatment and when depressive symptoms increased or persisted
- (d) a referral to an acute day hospital
- (e) an admittance to an inpatient hospital
- (f) a suicide or self-harm attempt

Information obtained from MHIS and hardcopy files was converted into quantifiable categories and processed in SPSS.

Survival analysis

This study centred on survival analysis. The outcome of interest was ‘the event’ – i.e. the relapse or recurrence of depression and ‘time to event’ – i.e. the length of time to relapse and/or recurrence of depression. Time to event comprised days, weeks, months or years from the beginning of the follow-up to the relapse or recurrence of depression. This required analyses of the data for Treatment I (Group CBT) and treatment II (Group Information and Support). All incompletely observed responses were censored (fixed type I censoring). Censored events consisted of all cases where participants did not experience recurrence of depression before the end of the follow up period, were discharged before the end of the follow up period, or were lost to follow up. Although more than one relapse or recurrence can occur for the specified period, for the purpose of this analysis only one event for relapse and one for recurrence were of designated interest. The descriptive methods included Life Tables, Survival Distribution and Kaplan-Meier Survival Curves. The comparison methods comprised Long-Rank Test (to compare the two survival curves) and Cox Regression Test.

Ethical considerations

Ethical approval for this study was sought and obtained from Provincial Ethics Committee, St. John of God Hospitaller Services in June 2011.

Ethical issues which may have arisen from this study were considered and addressed below:

- a. This study utilized previously collected data.
- b. No additional information was collected from any participants.
- c. An information letter was sent to all participants attending the treatment groups I and II, and consent forms were signed prior to conducting the study.
- d. All group participants have been advised of the voluntary nature of this study and that their participation or otherwise would in no way affect their treatment in Cluain Mhuire Services.
- e. No deception was used in the study.
- f. Confidentiality was maintained. The collected data is stored on an encrypted computer, with all hardcopy files maintained in locked cabinets by the Principal Clinical Psychologist. Access to the files is granted on a strictly need-to-know basis.
- g. Participants have been assured that no identifying information from questionnaires or files would be used when reporting results. To ensure confidentiality and anonymity, summary statistics only were provided.

Results

Participant demographic characteristics

The overall study sample (N=68) comprised 29 males (43%)

and 39 females (57%). For the entire sample, the socio economic status was as follows: employers and managers: 3 (4%); professional (higher, lower and other non-manual): 21 (31%); manual (skilled, semi-skilled and unskilled): 14 (21%); all other gainfully occupied and unknown: 5 (7%); full-time parent: 3 (4%); student: 9 (13%); unemployed: 9 (13%); retired: 1 (1%); sick leave: 2 (3%); FAS students: 3 (4%); and volunteers: 1 (1%).

Participant clinical characteristics

Prior to receiving treatment, 15% of the overall sample had a prior history of self-harm, 21% previously attempted suicide, 40% had a prior history of substance abuse, 28% were previously hospitalised, 56% received prior psychological input, and 44% attended an acute day hospital. The average age of the onset of depression was 26 for CBT group participants (M=25.74; SD=13.04) and 28 for Group Information & Support participants (M= 27.78; SD= 11.74).

Physical health issues

49% of the sample had a physical health issue or multiple issues (varying from chronic back pain, diabetes, epilepsy, IBS to chronic fatigue syndrome among other conditions), with the physical health record unavailable or incomplete for 40%.

Psychiatric Co-morbidity

Depression was a primary diagnosis for all participants (as per study inclusion criterion). Thirty five (51%) participants presented with a co-morbidity of another psychiatric condition, with the most common secondary diagnosis being anxiety (40%). Other co-morbid conditions comprised current or past addition (4%), psychosis (1%), eating disorder (1%), phobia (1%), and post-traumatic stress disorder (PTSD) (1%). 4% of the diagnostic impressions corresponded with an Axis II of the DSM IV (personality disorders). These were classified according to the SCID-I interview.

Pharmacological Treatment

Four participants (6%) were not prescribed any type of psychiatric medication at the commencement of treatment. Six participants (9%) used benzodiazepines; 63(93%) were on antidepressant medication; two (3%) used major tranquillisers; and 14 (20%) used other psychiatric medication at the start of their treatment.

Demographic and clinical characteristics of the Group CBT and Group Information & Support participants are presented in Table 1 below.

Table 1: Demographic & Clinical Characteristics.

Demographic & Clinical Characteristics					
Variables		Group CBT		Group Information & Support	
		N	%	N	%
Gender	Male	20	46.5	9	36
	Female	23	53.5	16	64
Age Group	18-24	-	-	1	4
	25-34	8	18.6	5	20
	35-44	11	25.6	9	36
	45-54	17	39.5	7	28
	55-64	7	16.3	3	12
Socio Economic Status	Employers and managers	3	4	-	-
	Professionals	12	28	9	36
	Manual	4	9.3	4	16
	Other	4	9.3	1	4
	Full-time Parent	3	7	-	-
	Student	6	14	3	12
	Unemployed	7	16.3	2	8

	Retired	-	-	1	4
	Sick Leave	-	-	2	8
	FAS Course	2	4.7	1	4
	Voluntary	-	-	1	4
Secondary Diagnosis	None	21	48.8	12	48
	Anxiety	17	39.5	10	40
	Personality	1	2.3	-	-
	Addiction	2	4.7	-	-
	Past Addiction	1	2.3	-	-
	Phobia	1	2.3	-	-
	Psychosis	-	-	1	4
	Eating Disorder	-	-	1	4
	PTSD	-	-	1	4
Axis II Diagnosis		2	4.7	1	4
Physical Health Issue		11	25.6	12	48
Prior Self Harm		5	11.6	5	20
Prior Suicide Attempts		9	20.9	5	20
Age of depression onset	0-9	3	7	1	4
	19-Oct	14	32.6	4	16
	20-29	9	20.9	10	40
	30-39	7	16.3	3	12
	40-49	7	16.3	4	16
	50-59	2	4.7	1	4
Prior Substance Abuse		16	37.2	11	44
Benzodiazepines*		4	9.3	2	8
Antidepressants*		39	90.7	24	96
Major Tranquilizers*		43	100	2	8
Other Psychiatric Medication**		10	23.3	4	16
Attended Psychiatric Hospital		11	25.6	8	32
Attended Day Hospital		21	48.8	9	36
Attended Psychological Therapy**		23	53.5	15	60

* = At Start of Treatment

** = Prior to Treatment

An independent- samples t- test was conducted to compare scores on BDI, BAI, CORE, WHO QoL and DAS at the assessment stage for Group CBT and Group Information & Support participants. There was no significant difference found between

the groups on any of the scores. Age of depression onset also did not differ significantly between the two treatment groups. Table 2 below displays means, standard deviations and t values of the pre-treatment characteristics for the two groups.

Table 2: Pre-Treatment Characteristics.

Pre-Treatment Characteristics					
Scores at Assessment	Group CBT		Group Information & Support		t
	M	SD	M	SD	
Age of depression onset	25.74	13.04	27.78	11.74	-0.63
BAI	16.74	9.86	21.6	13.93	-1.53
BDI	25.6	11.05	27.84	9.76	-0.84
CORE					
Wellbeing	2.05	0.75	2.31	0.96	-1.14
Problems	1.9	0.8	2	1.08	-0.36
Functioning	1.76	0.71	1.78	0.92	-0.06
Risk	0.42	0.42	0.39	0.49	0.2
Total	1.62	0.59	1.74	0.78	-0.72
WHO QoI					
Overall Quality of Life	2.86	1.01	2.62	0.82	0.97
Satisfaction with Health	2.44	1.07	2	1.21	1.52
Physical Health	21.74	5.34	20.04	5.45	1.24
Psychological Health	15.13	4.14	14.17	4.46	0.89
Social Relationships	7.86	2.42	7	2.3	1.42
Environment	26.45	5.65	25.79	5.1	0.47
DAS					
Externalised Self-esteem	32.86	9.25	33.63	11.91	-0.29
Analectic Self-esteem	19.44	5.39	19.25	7.01	0.13
Tentativeness	24.02	6.86	24.21	7.24	-0.1
Need for Approval	19	4.88	20.67	4.86	-1.34
Total	144.3	28.62	152.17	38.82	-0.95

Equality of variance

No statistically significant differences ($p>.05$) were found between the two treatment groups in relation to demographic and clinical characteristics such as gender, age, secondary diagnosis, physical health issues, prior suicide, prior self-harm, history of substance abuse, use of benzodiazepines at the start of treatment, use of antidepressants at the start of treatment, use of other psychiatric medication at the start of treatment, being admitted to a psychiatric hospital (inpatient), day hospital attendance, and previous use of psychological services. Levene's test of equality of variance for the two groups indicated that the homogeneity of variance assumption was not violated. However, there was a significant difference between Group CBT and Group Information & Support found on the BAI and CORE Problem Mean scores at the assessment.

Survival analysis

51% ($N=22$) in Group CBT and 52% ($N=13$) in Group Information & Support had a relapse of depressive symptoms during the first 6 months post-treatment, as indicated by their BDI-II scores at the monthly "booster" sessions and the retrospective file review. 44% ($N=19$) in CBT Group and 48% ($N=12$) in the Group Information & Support experienced a recurrence of depression.

54% of participants were categorized as right-censored cases (participants for whom the event of interest- i.e. recurrence of depression has not yet happened for the duration of the study or who were discharged from services and lost to the study during the time of interest). There were 24 censored cases in Group CBT and 13 in Group Information and Support.

Relapse of depression

Life tables - a descriptive procedure for exploring the distribution of time to event variables (i.e. relapse) was performed using monthly intervals to explore the relapse of depressive symptoms. 22 out of 43 participants in Group CBT and 13 out of 25 in Group Information & Support relapsed in the first six months post-treatment. Majority of participants (seven in Group CBT and four in Group Information & Support) experienced a relapse of depressive symptoms in the first month after their treatment completion. The lowest number of relapses occurred between third and fourth month with one participant in each group suffering from a relapse. Rates of relapse for the remaining months were: four in month 2, 5 and 6 and two in month 3 for Group CBT participants and two in month 2, 3, 5 and 6 for Group Information & Support participants. Group CBT and Group Information & Support relapse Life Tables displaying the interval time, proportion of terminating and surviving cases, cumulative proportion, probability density and hazard rates are listed in (Figure 1).

Although no major difference in survival curves between Group CBT and Group Information & Support can be observed, Group Information & Support has a slightly lower survival curve compared to the Group CBT curve. The highest and nearly identical drop in probability of survival can be observed in the first two months post-treatment for both groups.

The Wilcoxon (Gehan) test was used to determine the effect of the treatment group on relapse rates. The analysis yielded no statistically significant difference [Wilcoxon (Gehan)=.003, $p>.05$].

The average survival time to relapse was estimated using Kaplan-Meier method. For Group CBT, the average time to relapse was 3.13 months ($SD=.43$; 95% $CI=2.3$ to 3.96) compared to 3.08 months ($SD=.54$; 95% $CI=2.03$ to 4.13) for Group Information & Support. The log-rank (Mantel-Cox) test revealed no significant difference between the survival rates over time ($\chi^2=.03$, $p>.05$).

Time to the onset of relapse (measured in months) was further compared between Group CBT and Group Information & Support using Cox proportional hazards regression analysis, with treatment condition (Group CBT or Group Information & Support) as a categorical (indicator) variable. This analysis revealed no significant difference in the hazard of relapse for the two groups [Exp (B) = .95, $p>.05$].

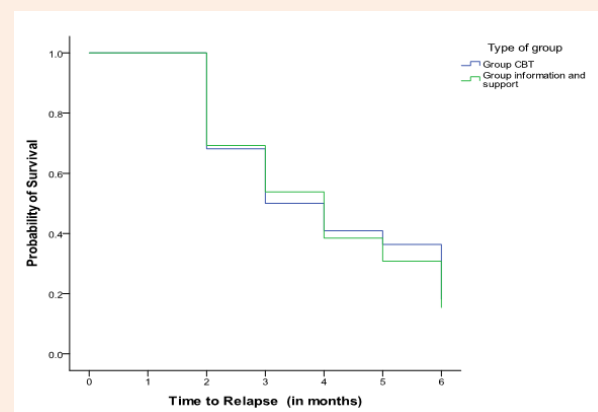


Figure 1: Relapse Survival Curves for Group CBT and Group Information & Support.

Recurrence of depression

Life table analysis performed for recurrence of depression displayed the number of participants in each group exposed to risk, after adjusting for right-censored cases. Time to recurrence of depression was divided into ten 7-month intervals (0- 63 months) for Group CBT and four 7-month intervals (0-21 months) for Group Information & support for convenience of analysing data.

19 (44%) participants in CBT Group suffered from a recurrence of depression compared to 13 (52%) in Group Information & Support. As the recurrence life tables indicate, the highest number of recurrence of depression occurred within the first 8 months post 'booster' sessions (six monthly follow-up sessions). 11 participants in Group CBT and four in Group Information & Support experienced an onset of a new episode of depression at that time (interval 7-14 months). During the interval 14-21 months, further two participants in Group CBT and six in Group Information & Support suffered a recurrence. Interval 21-28 saw three additional Group CBT participants experience a recurrence compared to two participants in Group Information & Support.

Three participants relapsed in the period between 21-63 months post-treatment (in intervals 21-28, 28-35 and 56-63) in Group CBT. There is no relapse data for Group Information & Support past 28 months (two last participants relapsed in interval 21-28months) (Figure 2).

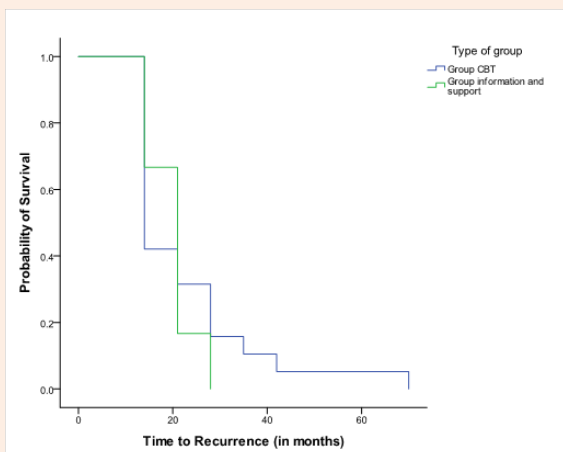


Figure 2: Recurrence Survival Curves for Group CBT and Group Information & Support.

There were minor differences only in survival curves for both treatment groups. There was a larger drop in probability of survival in the first recurrence interval (7-14 months) for Group CBT compared to Group Information & Support. In the second interval (14-21 months), the probability of survival decreased at a lower rate for Group CBT compared to Group Information & Support and continued at that level up to the final interval.

Wilcoxon (Gehan) test was conducted to compare the survival distribution for recurrence of depression for Group CBT and Group Information & Support participants, based on differences in group mean scores. Since the value of the test is $>.05$, it can be concluded that the Group CBT and Group Information and Support survival curves are not significantly different.

Kaplan-Meier survival analysis method was used to estimate time to recurrence in presence of right-censored cases. Survival time mean for Group CBT was 18.79 (SD=3.11; 95% CI=12.70 to 24.86) and for Group Information & Support was 15.92 (SD=1.64; 95% CI=12.69 to 19.14). Although no statistically significant difference in the average survival time was found between the two groups, Kaplan-Meier indicated a slightly higher average survival time for the Group CBT participants. Log Rank Test (Mantel-Cox) ($\chi^2=.67$, $p>.05$) conducted to examine equality of survival by weighting all time points indicated no statistically significant difference between the two survival functions.

Further exploration with Cox regression analysis, which controlled for the censored and uncensored data, indicated that Group CBT participants were .75 less likely to suffer a recurrence of depression than the Group Information & Support participants.

Discussion

The hypotheses for the current study were as follows: Group CBT would be more effective at reducing the number

and increasing the length of time to relapse and/or recurrence of depression compared to Group Information and Support. The findings did not support these hypotheses. There was only a slightly lower relapse rate for Group CBT participants (51% vs 52% in Group Information and Support) within the first six months post-treatment, as per relapse definition. The difference in the average length of time to relapse between the two groups was also minor and did not reach a level of significance (3.18 months for Group CBT and 3.03 months for Group Information and Support).

Similarly, the recurrence rates between the treatment conditions did not differ significantly, with findings indicating that 44% of participants in Group CBT experienced a recurrence of depression compared with 48% in Group Information and Support. The average time to recurrence of depression was 18.79 and 15.92 months respectively for Group CBT and Group Information and Support participants. Overall, the patterns of the survival functions are not essentially different.

These findings are comparable with results from some of the previous survival analysis studies exploring the effectiveness of different types of psychotherapy i.e. MBCT and CT for depressed adults [32,33,56]. Bockting et al. [33] reported a 72% cumulative relapse/recurrence rate for the treatment-as-usual (TAU) group compared with 46% for CT participants. A study carried out by Teasdale et al. [32] indicated a 40% relapse/recurrence rate for MBCT participants compared with 66% for TAU sample. The relapse rates in the current study were 51% and 52%, and recurrence rates were 44% and 48% for Group CBT and Group Information and Support respectively. These encouraging findings suggest that both group interventions may be effective in reducing the relapse and recurrence rates of depression. However, further prospective studies incorporating a control group are necessary to validate this claim.

It is of note that the majority of instances of relapse of depressive symptoms occurred imminently post treatment completion (first month). Similarly, the highest rates for recurrence of depression took place in the first six months after the follow-up sessions were completed. These findings suggest that participants should be carefully monitored at the time of reduction in the frequency of group meetings as well as at cessation of the follow-up group meetings, as these appear to increase some participants' vulnerability to symptom deterioration and/or subsequent depressive episodes.

Strengths and limitations of the current study

One of the limitations of the present study was a decrease of the sample size over time. Due to exclusion criteria, primary diagnosis being other than that of depression, group drop-out, non-attendance, or lack of access to the files, out of 244 initial participants only 68 met the inclusion criteria for this study. Although, the two treatment groups were relatively small, with 43 participants in Group CBT and 25 in Group Information and Support, there were no significant differences found between the groups on demographic and a variety of clinical characteristics at the start of the treatment.

Lack of a control group was another major limitation of this retrospective study. Despite initial attempts and an obtained ethical approval to include a control group in the study, due to

methodological issues and time constraints it became unfeasible to conduct the study in accordance with the original plan. Participants were also not randomly assigned to the group. After being assessed for the group, all individuals were wait-listed for the next available intervention (either CBT group therapy or Group Information and Support).

The design of the study did not permit for control of specific and non-specific factors which may have impacted the results. As noted by Moore et al. [20], when exploring the effectiveness of these groups for participants with bipolar affective disorder, the role of additional therapeutic input has not been investigated. Notably, 53.5% in Group CBT and 60% in Group Information and Support received psychological input prior to attending the group. It is unclear how many of participants continued to avail or commenced additional therapies within and outside of the service during the treatment and post-treatment. It can be argued that these may have served as a “buffer” against a subsequent relapse or recurrence of depression for some participants.

Similarly, majority of participants received pharmacological treatment at the commencement of the group (96%) and post-treatment (89.7%). Moore et al. [20] previously discussed the clinical and ethical difficulties in providing a “clean” sample which would not be exposed to any other psychological or pharmacological therapies except for the group. Since, a vast majority of participants received pharmacological and/or additional psychological treatment in addition to the group participation, the observed positive effects in reducing rates of relapse/recurrence and extending the length of time may not be solely attributable to the group interventions. On the other hand, there is also a likelihood that a reduction in use of antidepressant medication and/or discontinuation due to clinical improvement post-treatment, particularly if self-administered and abrupt, may have resulted in an increase in depressive symptoms which may have been interpreted as a relapse or recurrence of depression instead of discontinuation/withdrawal symptoms. This has been previously highlighted by Storosum et al. [34].

Lack of consistent definitions of ‘relapse’ and ‘recurrence’ of depression across the literature adds to the complexity of the issue. One of the key predictors of relapse of depression considered in previous studies is the number of prior depressive episodes. Previous studies found no prophylactic effect of cognitive-based therapies (i.e. MBCT) on the relapse and recurrence of depression in participants with only two prior episodes of depression when compared with TAU sample [32]. The same study highlighted the positive linear link between the number of depressive episodes (three or more) and the risk of relapse/recurrence of depression. This is in line with recent findings reported by Bockting et al. [33]. No significant protective effect of CT was observed in participants with only two previous episodes of depression. The study also indicated that a higher number of previous depressive episodes (five and more) were necessary for CT to produce significant positive results. The number of depressive episodes was difficult to ascertain in the present study, based on the retrospective file review, which may have obscured the findings. The diagnostic classification of many participants suggested ‘recurrent’ condition. Those who experienced three or more episodes of depression would have been at an increased risk of relapse/recurrence than those with two or less episodes, as indicated by Teasdale et al. [32].

Other risk factors for recurrence of depression include, but are not limited to, chronicity of the episode (i.e. more than two years), “double depression”, family history of mood disorders, comorbidities, and late onset of depression (over 60 years of age) [36] and residual symptoms [28]. There is a scope for further investigation of how these variables may impact on relapse/recurrence rates and length of time to the measured event in depressed individuals.

It is possible that the non-specific factors, such as additional attention and group participation, pointed out by Bockting et al. [33], also impacted findings. One explanation that can be offered for the non-significant difference in outcome measures for the two groups is the impact of the therapeutic factors as opposed to the type of the intervention alone. As identified by Yalom [21], these nine therapeutic factors, discussed earlier, that effect change would have been expected to be present in both groups.

The unequal psychiatric appointment intervals and differences in how the information was recorded posed a difficulty in the current study. Although the standard appointments were scheduled every three month, some participants were seen more frequently. This was particularly the case if new medication was prescribed or existing medication was augmented, if there were any concerns such as suicidal ideation or attempts, self-reported significant increase in symptoms and deterioration in functioning, or non-response to the antidepressant treatment. Those participants were likely to be offered priority appointments. Therefore, there was more extensive information recorded and available pertaining to those participants than others. It is not unlikely that relapse/recurrence episodes may have occurred for the latter but had naturally dissipated over time prior to the scheduled appointment. Such issues mentioned above are not uncommon in retrospective studies. Future prospective studies would be essential in addressing these limitations.

There was also a small number of clients who discontinued medication or did not use antidepressant medication, therefore would not have been under regular psychiatric supervision and for whom the psychiatric appointment notes were either sporadic or not available. There is a possibility of the true rate of recurrence of depression being underreported or the length of the time to recurrence not being captured accurately in these circumstances.

One of the major contributions of this study is the analysis method utilised. There are relatively few survival analysis studies conducted with depressed clients in a secondary mental health community setting and none of this type have been carried out in Ireland to the author’s knowledge. Recent years have witnessed a proliferation of group therapies. Since interventions in a group setting help reduce waiting lists, and are more financially viable, they have become increasingly attractive and, consequently, prompted research of their effectiveness.

Selection of the participant is one of the main strengths of the study and increases the external validity of the results. It allows for a real life research compared to studies carried out with a convenience sample of university students, private clients or media recruited participants, as noted by Moore et al. [20].

Non-restriction on medication status or exposure to other psychotherapies at entry and during treatment is quite a unique feature of both interventions and may have enhanced the generalis

ability of the study. As discussed earlier, it is also more clinically and ethically feasible. Bockting et al. [33] noted that most of the previous studies [32,33] only included participants who remained well after medication was discontinued at the entry assessment or who received the treatment of interest exclusively [33].

Participants in both groups were also checked for comparability on the pre-treatment characteristics, with no significant pre-treatment differences found on a number of demographic and clinical variables. Additionally, both groups were delivered by the same therapists, which reduced the confounding effects of the therapist characteristics on the study's findings.

Future studies

It would be essential to include a control group for future studies. Since it is unclear how effective both types of group are in preventing/decreasing relapse and recurrence in comparison to no treatment or TAU, an inclusion of an intent-to-treat control group (comprised of individuals who were referred to group therapy for depression but who did not respond to the invitation to arrange an assessment appointment) would facilitate a more comprehensive evaluation.

Future studies could also explore the role of mitigating factors, such as co-morbidity of depression with other psychiatric conditions and health issues. In the current study, 22 out of 43 CBT Group participants and 13 out of 25 in Group Support and Information met criteria for another co-morbid condition, according to SCID-I classification. These are high numbers and reflect the complexity of the presenting difficulties. However, the severity of these conditions and their effect on the relapse or recurrence of depression was not investigated. Co-morbidity, particularly of depression and anxiety, has been linked with an increased severity of depressive symptoms and poorer treatment outcomes [57-59]. In the present study, 40% of participants had a secondary diagnosis of anxiety, according to the SCID-I.

Physical health issues, which varied in their severity and chronicity, were recorded but not investigated in detail. As noted by Boland and Keller, research indicates that "comorbid medical illness predisposes individuals to a worse course of depression" and exacerbates their vulnerability to relapse or recurrence. Further Cox Regression analyses of co-morbid conditions and physical health issues as co-variants would determine whether there is a significant difference in relapse and recurrence hazards for these variables.

Conclusion

Results indicated a shift in the hypothesised direction for relapse and recurrence of depression, but were not of statistical significance. Group CBT and Group Information and Support appear to be equally effective in decreasing the number and increasing time to relapse and/or recurrence of depression.

Considering the burden that depression incurs at individual, familial, community and societal levels, on-going research of its effective treatments is crucial. It can be concluded that group interventions appear to reduce the rates of relapse and/or recurrence of depression in pharmacologically treated participants diagnosed with depressive disorder. Prospective studies, particularly addressing limitations of the current study and using a control group and a larger sample, are necessary.

References

1. Yin L, Chino T, Horst OV, Hacker BM, Clark EA, et al. (2010) Differential and coordinated expression of defensins and cytokines by gingival epithelial cells and dendritic cells in response to oral bacteria, *BMC Immunol* 11: 37.
2. Wistreich GA, Lechtman MD (1982) *Oral Microbiology*. (3rd edn), Macmillan Publishing Co INC., New York, pp. 582-595.
3. Ross PW (1979) *Infection of the mouth*. Clinical Bacteriology, Churchill-Livingstone, Edinberg, London, pp. 80-88.
4. Samaranyake LP, Jones BM (2002) *Essentials of Microbiology For Dentistry*. (2nd edn), Churchill-Livingstone, London, pp. 205-252.
5. Shnawa IMS (2015) The interplay of the local microbiome with oral mucosal compartment. *Am J Biomed and LifeScience* 3(4-1): 17-19.
6. Lever JD (1980) *Introducing Anatomy*. William Heinemann Medical Books Ltd., London, pp. 245-272.
7. Gartner LP, Hiatt JL, Strum JM (2003) *Cell Biology and Histology*. (4th edn), Lippincott Williams and Wilkins, Science Review, Philadelphia, p. 62-72.
8. Ross MH, Kaya GI, Pawlina W (2003) *Histology, A Text And Atlas with Cell And Molecular Biology*, (4th edn), Lippincott Williams And Wilkins, Philadelphia, USA, p. 19-78.
9. DiFiore MSH (1967) *An Atlas of Human Histology*. (3rd edn), Henry Kimpton, London, p. 16-29.
10. Owen JA, Punt J, Stranford SA, Jones PP (2013) *Kuby Immunology*. (7th edn), Mecomillan, England, pp. 105-140.
11. Abbas AK, Lichtman AH, Pillal S (2015) *Cellular and Molecular Immunology*. (8th edn), Elsevier Saunders, Canada, pp. 289-314.
12. Montovani A, Dinarello CA, Ghezzi P (2000) *Pharmacology of Cytokines*. Oxford university Press, Oxford, USA, p. 1-20.
13. Theze J (1999) *The cytokine network and Immune Functions*. Oxford University Press, Oxford, USA, pp. 1-13.
14. Paul WE (2003) *Fundamental Immunology*. (5th edn), Williams and Wilkins, Philadelphia, USA, pp. 685-841.
15. Steel C, Fidel PL Jr (2002) Cytokine and Chemokine produced by oral and vaginal epithelial cells in response to *Candida albicans*. *Infect Immun* 70(2): 577-583.
16. Schaller M, Boeld U, Oberbauer S, Hamm G, Hube B, et al. (2014) Polymorphonuclear leukocytes induce protective Th1 type cytokine response in an in-vitro model of oral candidiasis. *Microbiol* 150(9): 2807-2813.
17. Dongari - Begtzoglou A (2015) *Fungal Immunology*. In: Haffnage GB & Fidel PC (Eds.), *organ Perspective* 13-36.
18. Madianos PN, Kinane DF, Sandros J, Karlsson C, Lappin DF, et al. (2000) Cytokine response of oral epithelial cells to *Poryphyomonas gingivalis* infection. *J Dent Res* 79(10): 1808-1814.
19. Uehara A, Gugawara S, Takada H (2002) Priming of human oral epithelial cells by INFγ to secret cytokine in response and LPS, LTA, and peptidoglycan. *Med Microbiol* 51(8): 626-634.
20. Ohata K, Ishida Y, Fukui A, Nishi H, Takechi M, et al. (2014) TLR expression and TLR mediate IL8 production by human sub-mandibular gland epithelial cells. *Mol Med Rep* 10(5): 2377-2382.
21. Yilmaz O (2008) The chornichle of *Porphyromonas gingivalis*: The microbiome, the human epithelia, and their interplay. *Microbiol* 154: 2897-2903.

22. Wade WG (2013) Oral microbiome in health and disease. *Pharmacol Res* 69(1): 137-143.
23. Marsh PD (2006) Dental plaque as biofilm and microbial community implications for health and disease. *BMC Oral Health* 6(Suppl 1): S14.
24. Hesagawa Y, Tribble GD, Baker HV, Mans JJ, Handfield M, et al. (2008) Role of *Prophyromonas gingivalis* SerB in gingival epithelial cell cytoskeleton remodeling and cytokine production. *Infect Immun* 76(6): 2420-2427.
25. Marshal RI (2004) Gingival defensins: Linking innate and adaptive immune responses to dental plaque. *Periodontol* 35: 14-20.
26. Colombo AV, da Silva CM, Haffajee A, Colombo AP (2007) Identification of intracellular oral species within human cervicular epithelial cell from subject with chronic periodontitis by fluorescence in situ hybridization. *J Periodontal Res* 42(3): 236-243.
27. Colombo AV, Silva CM, Haffajee A, Colombo AP (2006) Identification of oral bacteria associated with cervicular epithelial cells from chronic periodontitis lesion. *J Med Microbiol* 55(Pt 5): 609-615.
28. Shnawa IMS (2015) Oral mucosal immune tolerance versus immune silencing. *AM J Biomed Lif Sci* 3(4-1): 7-9.
29. Versteeg J (1985) *A Colour Atlas of Virology*. Wolf Medical Publication Ltd., Netherland, p. 98-99.
30. Mat Tek Cooperation (2015) Automated barrier of an in-vitro oral epithelial model. Mat Tek Cooperation, USA.
31. Guggenhiem B, Gmur R, Galicia JC, Stathopoulou PG, Benkanakere MR, et al. (2009) In vitro modeling of host-parasite interactions: The sub-gingival bio-film challenge of primary human epithelial cells. *BMC Microbiol* 9: 280.