

## EXPERIENCES IN MIDDLE EASTERN POPULATIONS

# The Treatment Gap of Depression in Persons with Cancer

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### Abstract

The epidemiology of depression showed that the rates are high. For example, the World Mental Health Survey, an epidemiologic community study conducted in 28 countries, found a life-time prevalence rate that ranged from 3.3 % in Nigeria to 21.4% % in the US. With regard to persons with cancer, 12.5% of a sample of over 17,000 respondents over the age of 50 of a US survey of community-dwelling adults found that people that reported they had cancer had higher risk of fatigue (OR =1.5 95% CI 1.3-1.6); depression (OR=1.2, 95% CI 1.1-1.4) and pain (OR =1.2, 95% CI 1.03-1.3.).The rate of depression seems to be differently associated with cancer site. For example: It is higher in pancreatic cancer (33%-50%) and lung (11%-44%), and it is lower in lymphoma (8%-19%) and colon (13% and 25%). For breast cancer –likely the most studied cancer site- the prevalence ranges from 1.5% to 46%. Ciaramelli and Poli (2001) found that depressed persons had more pain and metastasis than the non-depressed but no more lifetime depression than the non-depressed. In terminally patients, studies have found that the higher the level of disability the higher the rates of depression. Interestingly, while almost all studies of depression in the community found higher rates in women than in men - this is far from the rule among persons with cancer. Despite the marked burden and the existence of effective treatment, a very large proportion of the persons with depression remain untreated. The causes to be imputed for the treatment gap are of different nature. Some of these causes are related to the suffering person, to the social context and to the health system. Often, the treating physicians fail to identify depression and to treat it properly. For example, in one evaluation of 456 outpatients with solid tumors a minority (14%) of the depressed were identified as such. Why is it important to assess depression in persons with cancer? Untreated depression both enhances the risks to life and it lowers the quality of life. It may be associated to a reduced chance of survival in women with early stage breast cancer. One possible reason is limited adherence to the treatment plan. Timely identification and well prescribed and conducted treatment could make a substantial difference.

**Keywords:** Depression - cancer - site-dependence - treatment - non-treatment impact

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### Introduction

#### *A Case for Action*

Unipolar depression ranks high in the global burden of disease, particularly in industrialized countries (World Health Organization, 2001). However, as the epidemiologic transition is setting in, developing countries may not be spared from such a burden. Almost in all countries where community-based epidemiologic studies have been conducted, depression was found to be common. For example, in the US, the life-term prevalence rate in the community was found to be about 20% (Kessler and Ustun, 2008). The World Mental Health Survey (WMHS), an epidemiologic study conducted in 28 countries that used the CIDI-Composite International Diagnostic Instrument to arrive at a psychiatric diagnosis, found that the life-term prevalence rate of any mood disorder, including unipolar depression, ranged from a low of 3.3 % (SE 0.3%), in Nigeria, to a high of 20.4% (SE 0.5%), in New Zealand. For Israel, the respective overall rate was 10.7% (SE 0.5). For Lebanon, another Middle Eastern country that participates in the WMHS, the life-term rates for any

mood disorder was 12.6% (SE 0.9%) (Kessler and Ustun, 2008). The WMHS also estimated 12-month prevalence rates; these ranged from a low of 1.1% (SE 0.2), in Nigeria, to a high of 9.7% (SE 0.4%), in the US. In Israel, the 12-month rates among the Arab-Israelis and the Jewish-Israelis, estimated by the local component of the WMHS (Levav et al., 2007), were 8.2% (95% CI 6.2-11.0) and 5.9% (95% CI 5.1-6.8), respectively. The respective rate for Lebanon was 6.8% (SE 0.7%) (Kessler and Ustun, 2008).

Importantly, aside from being a frequent disorder in the community, depression causes much suffering and disability. In addition depression is co-morbid with other disorders and raises the risk for mortality (Kessler et al., 2003). The mental pain could be so intense that the person may contemplate suicide - and even carry it out.

Often, the rate of depression in persons with cancer is even higher than in "healthy populations". The reasons are varied, including biological, such as the effect of treatment, and psychological, resulting from losses such as the limitation of function in different areas of life (Massie, 2004). The epidemiologic studies on the

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comorbidity of depression and cancer have been conducted in different countries and in a majority of settings of the specialized services (e.g., inpatient services, outpatient clinics), and in the community.

Ciamarella and Poli, in Italy, studied 100 persons recruited from the Pain Therapy and Palliative Care Unit of a general hospital. They used a clinical instrument, the SCID, to investigate depression and another instrument to investigate pain based on the McGill Pain Questionnaire. The authors found that 49 persons had depression. This percentage decreased to 28, when physical symptoms were replaced by other – "psychological"- items. Importantly, the persons diagnosed with depression did not have a life-time mood disorder more frequently than the current depression-free group (Ciamarella and Poli, 2002).

A more recent study, conducted in Norway, on inpatient persons with cancer (N=225), used screening scales to ascertain the presence of depression and anxiety (both disorders are frequently associated). They found that 12% of the persons interviewed had anxiety; 12%, depression; and 44%, had both. Of clinical interest, the group that had neither, 32%, had less pain than any of the other three (Utne et al., 2010).

Those results, in which depression is higher among persons with cancer than in no-cancer respondents, have been replicated in the community. For example, in the US, the 2000 data from the Health and Retirement Study (N= 17210), a survey of community-dwelling adults over the age of 50, yielded the following results: 12.5% of the sample reported they had cancer. This group had higher risk of depression, measured by CESD (OR=1.2, 95% CI 1.1-1.4), had more fatigue (OR=1.5 95% CI 1.3-1.6) and pain (OR =1.2, 95% CI 1.03-1.3) (Reyes-Gibbi et al., 2006).

Reviewers, however, have noted that the studies have been affected by methodological limitations, for example, a majority of studies used a variety of depression scales (e.g. the HDS-Hamilton Depression Scale (Hamilton, 1960) or the CESD-Center for Epidemiologic Studies (Hann et al., 1999)) that are not truly diagnostic. Even when those scales are carefully calibrated and thus able to split apart persons with a disorder from those disorder-free they do not generate a psychiatric diagnosis. Indeed, studies that relied on more valid diagnostic methods, such as standard diagnostic instruments (e.g., the CIDI-Composite International Diagnostic Instrument, as applied in the WMHS) are a few (Kessler and Ustun, 2004). In turn, some of the latter, despite the methodological improvement, are affected by the inclusion of symptoms that are "physical" in nature and therefore they may result from cancer rather than being a "true" expression of the mood disorder. (Endicott modified a diagnostic instrument and submitted replacements for those ambiguous diagnostic items (Endicott, 1984).) Despite the limitations, there is an inescapable conclusion: the prevalence rate of depression is high in persons with cancer and the impact is considerable. The rates by selected sites are as follows: oro-pharyngeal, 22%-77%; pancreatic, 33%-50%; breast, 1.5%-46%; colon, 13%-25%; and gynaecological, 12%-23% (Massie, 2004). With regard to the impact of

depression in persons with cancer McDaniel et al (1995) have noted that it is multiple and substantial, including reduction in the quality of life, reduced adherence to medical treatment and poorer outcome. Yet, "studies show that psychiatric disorder goes unrecognized and untreated" (Fallowfield et al., 2001).

#### *The Treatment Gap*

Despite the availability of rather efficacious means of intervention, such as antidepressant medications (Spijker and Nolen, 2010) and psychological methods, eg cognitive behavioral therapy (NICE, 2010), the treatment gap –the difference between the true and treated prevalence of depression (Kohn et al., 2004) - is frequent, while the treatment lag – the time from the onset of depression to the first contact –is considerable. With regard to the latter, the WMHS cited above found for all the participating countries that the median duration of delay in years among cases that subsequently made treatment contact ranged from a low of 1.1 (SE 0.3) to a high of 14.3 (SE 3.1). With regard to the treatment lag, a World Health Organization study found that world-wide at least 56% of the persons with a mood disorder are untreated (Kohn et al., 2004).

An analogous situation could be found among persons with cancer, including among those who undergo cancer care. Henceforth some selected facts: Hewitt and Rowland (2002) noted, in their community study (N=95615) conducted in the US, that individuals who reported that they had cancer (n=4878) used mental health services more often than those who were cancer-free. "Among individuals 18-44...14.0% of cancer survivors as compared with 6.5% of those without such a history reported having used a mental health service in the past year". But "a significantly higher proportion of cancer survivors as compared with those without such a history reported needing mental health services but not getting them because of cost ..." The unmet needs were not randomly distributed: the younger respondents; those with lower educational attainment; the never or those previously married; those without health insurance; and those belonging to disadvantaged ethnic groups had higher unmet needs.

In another study conducted among low-income women with breast or gynecological cancer (N= 472) receiving care in a public hospital in the US, 24% reported moderate-severe depressive disorder. Of this group, only 12% of women received antidepressant medication while 5% reported seeing a counselor or participating in a support group (Eli et al., 2005). Obviously, many factors operate to determine the treatment gap.

In the general population those factors have been grouped as both objective and subjective (Kohn et al., 2004). With regard to the former (the three factors mentioned heretofore do not constitute an exhaustive list), the lack of availability or accessibility of the services are a formidable objective barrier to their use. Also, if services are not tailored to the specific population in need, such as in terms of gender or culture, the potential users or their families may stay away from them. Lastly, the untreated prevalence may not be reduced if the physician is unable

to recognize or treat depression or holds a negative attitude towards psychological disorders. The subjective factors are of a diverse nature, such as stigma, that may prevent seeking care or cause aborting prematurely a course of treatment.

In the case of cancer all of those factors may operate, and even be further compounded by other (proximal and distant) causes. These factors are of a different nature according to the stage of the disorder and the setting of care, e.g., specialized services or primary care—at the stage of follow up or remission. The availability, knowledge and attitudes of the practitioners are markedly different in all those settings. Greenberg, in the US, grouped the barriers to care arising from both uncertainty and cost. For her, uncertainty reflects the difficulties in identifying and defining depression in the context of cancer, where sadness and distress could be understood as a natural reaction to a difficult predicament. This a priori assumption hinders both the ability of the treating physician to perceive the psychiatric disorder and of the person with cancer to ask for the appropriate care. Consequently, people with depression remain undiagnosed and not cared, with the ensuing risks (e.g., in the final stages of cancer, undiagnosed and untreated depression may result in earlier entry into a hospice (Christakis, 1994)).

Costs, notes Greenberg (2004), constitute an important barrier, particularly for countries where the health insurance coverage for mental health care is limited. Much less often mentioned in the relevant literature is that depression, with or without comorbid anxiety, may not only affect the person with cancer but the caretaker as well. Good practice calls for a double concern -patient and caretaker- and not for just one member of the dyad.

## Recommendations

Obviously, recommendations purported to reduce both the treatment gap and lag depend on both the level of action that would assure to bring maximum change as well as on the feasibility of their implementation.

Two examples, both at the system and at the clinical levels illustrate the above. At the system level, if the barrier to care is caused by the limited or total lack of availability and accessibility of the mental health services, planning and administrative actions ought to be taking to dismantle those barriers. But, if the chief barrier is located at the clinical level then a routine procedure should be devised to both detect and treat those persons with depression. If rational decisions are adopted following a diagnosis, for example, of the location and type of the barriers, there is a good chance that the treatment gap and lag could be shortened to the benefit of the psychological status of the person with cancer and, hopefully, for the outcome of the medical care.

## References

Christakis NA (1994). Timing of referral of terminally ill patients to an outpatient hospice. *J Gen Intern Med*, **9**, 314-20.  
Ciaramella A, Poli P (2001). Assessment of depression among

*The Treatment Gap of Depression in Persons with Cancer* cancer patients: The role of pain, cancer type and treatment. *Psycho-Oncol*, **10**, 156-65.  
Eli K, Sanchez K, Vourlekis B, et al (2005). Depression, correlates of depression, and receipt of depression care among low-income women with breast or gynecological cancer. *J Clin Oncol*, **23**, 3052-60.  
Endicott J (1984). Measurement of depression in patients with cancer. *Cancer*, **53**, 2243-9.  
Fallowfield L, Ratcliffe D, Jenkins V, et al (2001). Psychiatric morbidity and its recognition by doctors in patients with cancer. *Br J Cancer*, **84**, 1011-5.  
Greenberg DB (2004). Barriers to the treatment of depression in cancer patients. *J Natl Cancer Inst Monogr*, **32**, 127-35.  
Hamilton M (1960). A rating scale for depression. *J Neurology Neurosurgery Psychiatry*, **23**, 56-62.  
Hann D, Winter K, Jacobsen P (1999). Measurement of depressive symptoms in cancer patients: Evaluation of the Center for Epidemiological Studies Depression Scale (CES-D). *J Psychosom Res*, **46**, 437-43.  
Hewitt M, Rowland JH (2002). Mental health service use among adult cancer survivors: Analyses of the National Health Interview Survey. *J Clin Oncol*, **20**, 4581-490.  
Kessler R, Berglund P, Bessler O, et al (2003). The epidemiology of major depressive disorder. *JAMA*, **289**, 3095-4105.  
Kessler RC, Ustun TB (2004). The World Mental Health (WMH) Survey Initiative. Version of the World Health Organization (WHO) Composite International Diagnostic Interview (CIDI). *Int J Meth Psych Res*, **13**, 93-121.  
Kessler R, Ustun BT (2008). The WHO World Mental Health Survey. Global perspectives on the epidemiology of mental disorders. New York: Cambridge University Press.  
Kohn R, Saxena S, Levav I, et al (2004). The treatment gap in mental health care. *Bull World Health Org*, **82**, 858-66.  
Levav I, Al-Krenawi A, Ifrah A, et al (2007). Common mental disorders among Israeli Arabs. *Israel J Psychiatry*, **2**, 104-113.  
Massie MJ (2004). Prevalence of depression in patients with cancer. *J Natl Cancer Inst Monogr*, **32**, 57-71.  
McDaniel JS, Musselman DL, Porter MR, et al (1995). Depression in patients with cancer. Diagnosis, biology and treatment. *Arch Gen Psychiatry*, **52**, 89-99.  
NICE (2004). Depression: management of depression in primary and secondary care. NICE guideline December . [www.nice.org.uk/guidance/index](http://www.nice.org.uk/guidance/index) Accessed February 2010.  
Reyes-Gibbi CC, Aday LA, Anderson KO, et al (2006). Pain, depression, and fatigue in community-dwelling adults with and without a history of cancer. *J Pain Symptom Manage*, **32**, 118-28.  
Spijker J, Nolen WA (2010). An algorithm for the pharmacological treatment of depression. *Acta Psych Scand*, **121**, 180-9.  
Utne I, Miasowski C, Bjordal K, et al (2010). The relationship between mood disturbances and pain, hope, and quality of life in hospitalized cancer patients with pain on regularly scheduled opioid analgesic. *J Palliat Med*, (in press).  
World Health Organization (2001). World Health Report 2001, New understanding-New hope. Geneva: World Health Organization.

