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XXIV CICLO

A theoretical and empirical contribution to the study of the psychological factors that may predict faster HIV progression within a psychoimmunology and health psychology prospective

Tutor: Prof.ssa Patrizia Steca

Tesi di dottorato di:

Andrea Norcini Pala

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This work is dedicated to my precious niece Zoe. With the words of grandmother Elia: "I want you to have something to remember me" and I hope this will inspire you to make of the world a better place.

All the elements of a system must work in concert to achieve a goal. I personally consider this work as the goal of a system of which I have been just a part. Therefore, I must be thankful to many persons that have inspired and supported me. Thank you!

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1. Psychoneuroimmunology

In this chapter the basis of psychoimmunology will be introduced and the more relevant studies conducted so far will be presented together with the evidence about the connection between psychosocial factors and the immune system functioning. In addition, there will be presented the evidence about the connection between the same psychosocial factors, and mental and physical health, considering their behavioral pathways.

1.1 Introduction

Einstein (quoted in Nash 1963, p. 173) claimed, “the grand aim of all science [...] is to cover the greatest possible number of empirical facts by logical deductions from the smallest possible number of hypotheses or axioms." In fact, researchers who aim to understand the phenomena observed among human beings inevitably deal with complexity, but they generally adopt a reductionist explanatory approach. For instance, they may hypothesize linear associations between variables but this approach might be not adequate to fully explain and understand the complexity of bio-psychological systems such as human beings. Furthermore, the participants to the studies are not living in social vacuums but they rather live in macro and micro systems in which they are strictly ad inextricably involved in social interactions, and are influenced by laws and cultural, moral, and religious principles. Thereby, several variables may simultaneously act on human beings and, since it is very unlikely to control all of these aspects, the act of simplifying a complex system of interactions to a linear relationship might be too hazardous. Thus, it may be more appropriate to

adopt the axiom of circularity drawn by the systemic theory that states each element of a system to influence and simultaneously to be influenced by the elements of the same system (e.g., Bateson, 1968, p. 173). Accordingly, complexity of human beings may be better represented by circular relationships rather than by unidirectional linear “arrows.” These premises could be considered a general introduction to psychoimmunology, which is a branch of science raised from the fusion of several disciplines such as psychology, sociology, neurology, endocrinology, and immunology. Circularity, or reciprocity, is clearly confirmed by the mutual communication between the immune system, the endocrine system and the nervous system (Biondi, 1997) and then, for instance, “neuroticism,” a personality trait (psychology), might be associated with greater circulating cortisol (endocrinology), which may reduce immunological response (immunology). Likewise, cortisol may drastically increase the risk of depression (psychiatry/neurology), which might lead to social isolation; this could be considered an example of circular relationships that simultaneously involve different systems.

The study of complexity or complex models that involve multiple systems may be found, for instance, in Cannon (1929) who observed association of emotional state with the movements of the stomach and Selye (1956) who showed interest in multiple systems interaction, identifying the “general adaptation syndrome.” The author, for instance claimed that such a syndrome unifies a pattern of observations that were apparently unrelated (Selye, 1950, p. 4667). Solomon and Moos (1964), then, used the term *psychoimmunology* in their milestone work entitled "Emotions, immunity, and disease: a speculative theoretical integration." Subsequently Ader (1980) claimed *all* the physical illnesses to be ultimately affected by psychological factors stating that there is no exception but rather just different extent of influence. Currently, after

more than 30 years, we have the scientific confirmation that the relationship between the immune system and the brain exists. In addition, the underlying pathways are also known or at least hypothesized. The recent psychoimmunological studies are focused on several clinical phenomena such as autoimmune syndromes, infectious diseases, stress related disorders, depression, and chronic fatigue syndrome (e.g., Bull, Pariante, Huezo-Diaz, Aitchison, & Cleare, 2008; Pariante & Lightman, 2008). To some extent, these phenomena share a common aspect, namely the pronounced activation of the immune system as claimed by Raison and Miller (2001) about the illnesses associated with the immune system alteration, such as cancer and infectious diseases, which might be accompanied by psychological and behavioral features like depressed mood. Likewise, the Crohn's disease, or the irritable bowel syndrome, is associated with greater inflammation and immunological alteration, as well as with depression or/and anxiety (Kurina, Goldacre, Yeates, & Gill, 2001).

Psychoimmunology studies have also paid great attention to the concept of stress and the immune system activation; such a concept is undoubtedly multifaceted and involves behavioral, psychological, and physiological aspects. The construct of stress can be better understood by defining it in relation to the "homeostasis," namely a condition emerging from the interaction of psycho-behavioral, neural and endocrine (or neuroendocrine), and immunological systems (Ader, 1996; see also Selye, 1956). The concept of homeostasis effectively reinforces the importance of the interaction between immune system and mental functioning, together with the need to adopt a more complex approach. This relationship is currently known to be mediated by immune cells (e.g., macrophages) and their "communicators" (e.g., cytokines) as well as by endocrinological changes (e.g., cortisol production). Such physiological pathways may explain, for instance, the influence of the immune system on the brain as described by Dantzer et al. (2008) in a manuscript emblematically entitled "From

inflammation to sickness and depression: When the immune system subjugates the brain." However, there may be an influence through the opposite direction as well, namely from the brain towards the immune system, through the Central Nervous System CNS (e.g., mediated by epinephrine and norepinephrine) and the Hypothalamic-Pituitary-Adrenal axis HPA (e.g., through the cortisol). This pathway has been discussed by Cole (2008) in his paper entitled "Psychosocial influences on hiv-1 disease progression: Neural, endocrine, and virologic mechanisms" where the author discuss how psychosocial stressors can influence immune system functioning. These two papers provided information that can be summarized as follows: the infections caused by virus or bacterial, produce immune response as a functional reaction to fight the pathogen agent. The macrophages (from the greek: *makros* = large and *phagein* = eat), which are the first line immune system cells, are primarily activated since their action is actually to phagocyte the pathogens and then, they activate other leucocytes triggering the immune response. Macrophages, symbolically, "communicate" the state of infection through the cytokines and the brain perceives this status of sickness for the increased level of circulating cytokines (Dantzer et al., 2008). Likewise, several psychological variables (e.g., emotions and perceived stress) may stimulate the HPA and the nervous system triggering an endocrinological response that affects the immune system cells (Cole, 2008) and cytokines (Temoshok et al., 2008). There is evidence that cytokines and endocrinological response (e.g., cortisol production) mediate the relationship between the immune system and the nervous system as well as in exacerbating mental and physical diseases. Such observations, however, remains at physiological and intrapsychological levels, whereas human beings are rather gregarious and deeply involved in social systems throughout their life. The systemic theory and the discipline of social psychology have widely investigated this assumption, providing

evidence about the utility of considering the individual as a single element of a system and at the same time as a partner of dyadic relationships, as part of social groups, and as an *actor* influenced by social rules. The study of human beings should adopt many different "points of view" such as the physiological, intra-psychological, inter-psychological, and social perspective as well since an individual is part of social groups; therefore, there is no reason to exclude the social level. The social group(s) is/are part of a greater system and the human beings-related phenomena may be not exhaustively addressed by adopting a reductionist/linear approach. Onnis (1993), in a Batesonian perspective claimed the indivisibility of the mind, body, and environment, also mentioning the concept of homeostasis of the systems. The author stated that the stasis is kept when there is a change on each of its part; in other words, the homeostasis is ensured when after a perturbing event, every part of the system is willing to a change. Thus, in this perspective, the illness diagnosis may represent a perturbing event, and its influence can be observed physiologically, psychologically, behaviorally, and socially. HIV/AIDS for instance, is caused by the infection of HIV-1 virus that acts, indeed, physiologically on the immune system as well as on individuals' mental health; besides, the cognitions associated with the HIV/AIDS, e.g., the illness perception, could influence the patients' reactions as well, even promoting depression and/or discomfort. Furthermore, there may be social influences on such cognitive representations and the reactions derived from social stigma that is associated with HIV infection, and this may lead the individual to isolate because of the fear of rejection. Thereby, this example underlines the need of a definition of homeostasis that overcomes the limits of a biological approach and that embraces the individuals holistically rather than reductionalistically. This approach has been encouraged by Suls and Rothman (2004) in their manuscript "Evolution of the Biopsychosocial Model: Prospects and Challenges for Health Psychology" where

the authors emphasized the need to understand and utilize linkages among biological, psychological, social, and macro/cultural variables. Thereby, a multisystem, multilevel, and multivariate approach could lead to a better comprehension of health-related topics, also guided by transdisciplinary contributions, and based on the biopsychosocial perspective.

The present work is focused on HIV/AIDS infection, therefore, the following chapters are entirely devoted to this pathology, however, following above a briefly introduction of psychoimmunology is presented. Here, it is important to clarify that the psychoimmunology prospective and the integrated approach proposed fit with the study of HIV infection, as it is a chronic disease that can be controlled but still not cured. The chronicity and the involvement of the immune system make of the illness a delicate issue, especially for the psychosocial related aspects; thus, a holistic investigation that comprises physiology, psychology, socially and behaviorally reactions seems to be more than appropriate. This could help to understand which are the factors that are associated with a faster progression of the infection as well as with a more favorable (or unfavorable) mental and physical health.

1.2 The concept of stress

Selye (1950) discussed the construct of stress within the biological concept of general adaptation syndrome, which consists in a pattern of adaptive reactions to *non-specific* stress, namely every kind of stressor (e.g., mechanic, biological, social, as well as psychological) might potentially exacerbate the same reactions. However, there might certainly be specific reactions to different stressors (e.g., the fever in response to an infection, and the bodily temperature adjustment for adaptation to cold). The

general adaptation syndrome consists in three stages: the alarm reaction, the stage of resistance, and the stage of exhaustion; the changes observed in the first phase (e.g., catabolism) are reversed within the second stage but reappear in the last stage. In line with Selye (1950), this suggests that the ability to adapt to stress depends on the organism's resources and how well, and how long, it resists to stress, also considering that the resources are *finite* and genetically determined; therefore, exhaustion might eventually occur.

The physiological reactions to stress consist in a shift in hormonal production exemplified by the reduction of hormones that are not essential for the maintenance of life while and emergency is occurring, it is instead observed an increased level of adrenocorticotropin (A.C.T.H), produced by the pituitary gland (HPA axis), and that rises the level of glucocorticoids. The shift is essentially adaptive and necessary to deal with stress. However, Sapolsky (1999) claimed that the definition of stressors is fundamental to explain the effects of glucocorticoids and one major aspect to address is the duration of stress. If the stressors are acute, glucocorticoids are essential to cope with stress, whereas if the stressors are chronic the effect of glucocorticoids is detrimental and their effect can be either transient (e.g., memory loss) or more permanent (e.g., neurons loss; Sapolsky, 1999). Besides, the differences between acute and chronic cortisol production explains why acute reaction if functional for contrasting an infection, whereas chronic production of cortisol results in, e.g., immunosuppression (Dhabhar, 2000). Thereby, stress is a non-specific reaction to adverse conditions and the consequent changes observed may be adaptive, on acute reactions, but may be deleterious if the stressful condition is chronic. The detrimental effect of cortisol may be linked to the exhaustion stage, which occurs after the stage of resistance, namely when the genetically limited resources are consumed. Chronic

stress negatively affects the immune system not only through cortisol, in fact, if chronically solicited and activated, lymphocytes (the immune cells) lose their ability to fight infections or heal wounds. The "telomere" is the terminal portion of the DNA and it prevents the loss of genetic information during DNA replication, the chronic activation and senescence (aging), instead, lead to the loss or significant reduction of the telomere portion (Akbar & Vukmanovic-Stejic, 2007). Consequently, lymphocytes proliferation can be reduced with greater vulnerability of the organism; the same mechanism can be observed in HIV-positive individuals (Effros, 2007) as well as in those who experience chronic emotional stress (Epel et al., 2004). Interestingly, then, either a mechanical stressor (e.g., a virus) or psychological stressor (e.g., emotions) may lead to immune system functioning impairment. However, lymphocytes could also lose the ability to fight infections consequently to production of cortisol (acute and chronic) since it activates the TDO (Tryptophan 2,3-dioxygenase) enzyme that causes tryptophan depletion and the production of "kynurenine," the tryptophan metabolite (Zunszain, Anacker, Cattaneo, Carvalho, & Pariante, 2011). This metabolite reduces the immune system functioning (Fallarino et al., 2003) and increases the risk of depression (Zunszain et al., 2011) thereby chronic stress may be associated with greater vulnerability to external pathogens as well as with greater mental disorders (e.g., depression). For instance, the individuals suffering from psoriasis (a skin disease), may show cortisol dysregulation (Evers et al., 2010) and greater depression levels (Devrimci-Ozguven, Kundakci, Kumbasar, & Boyvat, 2002); furthermore, psoriasis is associated with greater difficulties with interpersonal relationships, and is greatly associated with stigma, because of its signs visibility. Therefore, physiological pathways as well as psychosocial mechanisms may impair patients' health. Another example is that about irritable bowel syndrome, which is associated with dysregulation of the daily production of cortisol, greater fatigue, and

physical symptoms of stress (Patacchioli, Angelucci, Dellerba, Monnazzi, & Leri, 2001). In addition, symptoms severity and endocrine dysregulation may be exaggerated by mental stress (Posserud et al., 2004). Thereby, it might be far too hard to separate the effects of psychosocial factors from the physiological ones. Hence, to elucidate the connection between psychological factors, genetic and physiological aspects it might be helpful to cite the concept of diathesis-stress. According to Bootzin and Acocella (1984), the diathesis-stress models typically articulate specific diatheses (from the greek *diáthesis* namely vulnerability, e.g., genetic predisposition) and propose non-specific stressors furthermore, Rosenthal (1970), among others, promulgated the notion that the behavioral expression of the biological vulnerability for schizophrenia was influenced by the exposure to stress. Thereby, individuals may be genetically predisposed to schizophrenia and could show the related symptoms as a consequence of the exposure to stressful conditions. Psychological factors, stress, physiological patterns, and genetic predisposition, might all inextricably interact and determine health outcomes. Nonetheless, the physiological effect of stress may be extremely important, especially in the context of HIV since the immune system may be further impaired, and stress represents, then, an additional threat that may worsen an already compromised health status. Furthermore, the stress-related increased risk of mental disorders may also impair health; hence, the concept of stress needs particular attention in the context of HIV care.

1.3 The immune system's messengers: The cytokines

The activation of immune cells, such as the macrophages, in response to pathogen infection produces a chain of events that may affect individuals' physical and mental

health. The *cytokine* (from the greek *cyto* = cell and *kinos* = movement) produced by immune cells, as well as, i.e., adipocytes, have showed to mediate this chain of events (Fried, Bunkin, & Greenberg, 1998); thereby, HIV-1 virus infection, for instance, activates macrophages that promote the immunological response by releasing cytokines (Peters, 1996). Two types of cytokine may be produced, the pro-inflammatory or anti-inflammatory that exert opposite actions: pro-inflammatory cytokines stimulate the inflammation, whereas anti-inflammatory cytokines reduce the inflammation (Elenkov & Chrousos, 2002; Fiorentino et al., 1991). Nonetheless, Il-6, which is principally pro-inflammatory, could also exert an anti-inflammatory effect by stimulating the release of anti-inflammatory cytokines such as the Il-10 (Petersen & Pedersen, 2005). Despite the intricate functioning of the cytokines network, it responds to the general rule of homeostasis and self-regulation of biological systems and, for instance, after an infection, the biological system tries to reestablish homeostasis by changing its internal conformation (cf. Bateson, 1968), e.g., through the migration and activation of macrophages and leucocytes. The inflammatory response subsequent to the virus infection recalls, for some extent, the "alarm reaction" of the general adaption syndrome (Selye, 1950) and since a greater level of inflammation may be too demanding for the organism, the Il-10 might be released in order to reduce the inflammation (Fiorentino et al., 1991). This could be hypothetically compared to the "resistance stage," where the first changes occurred within the alarm stage are reversed except when the infection and the inflammatory response are chronic. In fact, HIV-1 virus has the glycoprotein 120 (gp120) on its external envelope surface, which is able to locate the host cells target (e.g., macrophages). This increases the production of both TNF-α and Il-1 for the activation of macrophages (Barak et al., 2002) and the HIV-1 infection generates a chronic dysregulation in the cytokines network (e.g., greater pro-inflammatory), with

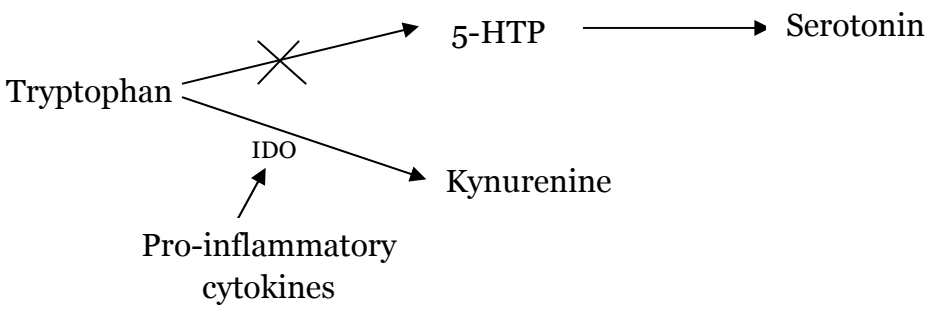
consequent detrimental effect on health such as a faster HIV progression (Li, Yim, & Lau, 2010). In fact, pro-inflammatory cytokines are produced in response to the infection but are also able to stimulate the replication of the virus (Poli et al., 1990; Poli et al., 1990). Furthermore, greater chronic inflammation is associated with neurological impairment in HIV positive patients (Barak et al., 2002) as well as greater risk of cancer (Grivennikov & Karin, 2011) and depression (Zunszain et al., 2011). Moreover, pro-inflammatory cytokines may act through another pathway, namely through the activation of the IDO enzyme (indoleamine 2, 3-dioxygenase; whereas cortisol activates TDO enzyme), which increases the level of kynurenine (Fallarino et al., 2003). Taken together, the chronic inflammation caused by the HIV-1 infection might be extremely dangerous since increased inflammation on the short time (acute phase) might be functional but the chronic inflammation is extremely harmful (Dinarello, 2006) and could impair patients' physical and mental health.

1.4 From the immune system to the brain: The sickness behavior

Cytokines dysregulation affects the body as well as the brain, as demonstrated by the fact that who suffers from an inflammatory illness (e.g., Crohn's disease, HIV/AIDS, cancer, or influenza) experiences physical symptoms (e.g., pain, swelling, redness, and fever in case of influenza) and psychological symptoms. The common influenza, in fact, is generally accompanied by lethargy, depressed mood, anhedonia, cognitive dysfunction, anxiety, fatigue, anorexia, sleep alterations, and increased sensitivity to pain (Capuron et al., 2002; Capuron & Miller, 2011; Dantzer et al., 2008). This is the consequence of the immune effectors' action (e.g., macrophages and cytokines) and the psycho-behavioral manifestations are part of the symptomatology of the "sickness-behavior" that has been found to be caused by cytokines and cortisol (Dantzer et al., 2008). More precisely, the depletion of the tryptophan and the

consequent lowered level of serotonin lead to such a depression-like manifestation, which is actually thought to be functional to fight the infection, since through this psycho-behavioral mechanism the organism acts to reduce the pathogen load or minimizing its damage (Raberg, Graham, & Read, 2009). The chronic activation of the immune system, and the consequent chronic cytokine-induced inflammation, may, instead, adversely affect health by promoting, e.g., ageing, and possibly depression. Hence, the differentiation between "acute" and "chronic" is crucial to predict favorable (or functional) or unfavorable (or dysfunctional) consequences. As hinted above, sickness behavior is linked to circulating pro-inflammatory cytokines and tryptophan depletion, and mostly characterizes medically ill individuals rather than medically healthy populations (Raison, Capuron, & Miller, 2006). The symptoms of sickness-behavior essentially resemble those of major depression, also in line with the evidence about the activation of the immune system in depressed individuals (e.g., Dantzer et al., 2008; Raison et al., 2006). In fact, the administration of cytokines such as TNF-α , Il-1, and Il-6 induced depressive-like behaviors in animals and humans (Brydon, Harrison, Walker, Steptoe, & Critchley, 2008); accordingly, the inhibition of pro-inflammatory cytokines resulted, instead, in a significant mood improvement (Tyring et al., 2006). These evidences, then, support the assumption of the role of cytokines in promoting depression strongly reinforced by the literature about patients undergoing IFN (interferon, a pro-inflammatory cytokine) treatment for hepatitis or cancer that confirmed the development of depressive symptoms caused by the treatment. In figure 1, we graphically exemplified the pathway through which pro-inflammatory cytokines promote tryptophan depletion.

Figure 1 – Depletion of tryptophan by pro-inflammatory cytokines.



5-hydroxytryptophan (5-HTP); indoleamine 2,3-dioxygenase (IDO)

Pro-inflammatory cytokines act reducing the level of 5-hydroxytryptophan, the intermediate metabolite that should eventually be transformed into serotonin (Capuron & Miller, 2004; Musselman et al., 2001). Despite the substantial overlapping symptomatology, cytokine-induced and idiopathic depression might still show relevant differences, namely cytokine-induced depression may be characterized by greater psychomotor symptoms (e.g., slower movements) and fatigue as well as the lack of guilt, respect to idiopathic depression (Capuron et al., 2009; Capuron et al., 2001; Felger et al., 2007; Majer et al., 2008). Interestingly, Capuron et al. (2009) suggested that the lack of guilt might be to consequence of the external locus of control of the emotional distress source (Kendler, Myers, & Zisook, 2008). Namely, HCV-positive (Hepatitis C Virus) patients individuate the cause of their depression in the IFN therapy, an external "agent." HIV-positive individuals, instead, there may be certain differences; the risk of sickness-behavior is of course drastically increased for the chronic inflammation that they experience (Lawson, Kelley, & Dantzer, 2011; Leserman, 2003). Even though, psycho-social factors such as stigma, guilt, and loneliness may still play a role in promoting depression (Rodkjaer, Laursen, Balle, & Sodemann, 2010). Hence, for the cytokines dysregulation and the psychosocial

factors associated with the diagnosis, HIV-positive individuals may be at greater risk for severe mental and physical health impairment.

1.5 Emotions and the immune system

The pioneer scientist in psychoimmunology G. F. Solomon (Solomon, Temoshok, O'Leary, & Zich, 1987; Solomon, Levine, & Kraft, 1968; Solomon & Moos, 1964) was one of the first to claim stress and emotions to affect illness physiologically through the humoral (immunity) and the nervous (SNC) pathways. Chronic stress, indeed, exerts an immunosuppressive action (cf. § 1.2) and emotions may favorite this effect through the physiological (e.g., catecholamine and cortisol) and the behavioral (e.g., dysfunctional behaviors) pathways. Accordingly, emotions deserve greater attention in the context of psychoimmunology and certainly, they should be defined and operationalized precisely (Frijda, 1987; Izard, 2010). In fact, although some authors (e.g., Frijda, Markam, Sato, & Wiers, 1995) consider emotions "what people say they are," emotions should be defined more scientifically, also drawing notions from many different disciplines. Kleinginna P. and Kleinginna A. (1981, p. 355), for instance, defined the emotions as "[…] a complex set of interactions among subjective and objective factors, mediated by neural-hormonal systems, which can (a) give rise to affective experiences such as feelings of arousal, pleasure/displeasure; (b) generate cognitive processes such as emotionally relevant perceptual effects, appraisals, labeling processes; (c) activate widespread physiological adjustments to the arousing conditions; and (d) lead to behavior that is often, but not always, expressive, goal-directed, and adaptive." Then, more recently, Izard (2010) supported this definition and claimed the need to integrate different definitions of emotions in order to account for their complexity. More precisely, the author stated:

"Emotion consists of neural circuits (that are at least partially dedicated), response systems, and a feeling state/process that motivates and organizes cognition and action. Emotion also provides information to the person experiencing it, and may include antecedent cognitive appraisals and ongoing cognition including an interpretation of its feeling state, expressions or social-communicative signals, and may motivate approach or avoidant behavior, exercise control/regulation of responses, and be social or relational in nature" (Izard, 2010; p. 367). These definitions underline the importance of a multidisciplinary approach to fully understand the construct of emotions; in addition, although emotions and mood have been quite often used as synonymous, generating greater confusion, they substantially differ (e.g., Davidson, 2001). Depression, for instance, is frequently mentioned as an emotion but it rather describes a mood state. Compared to mood, emotions are more intense, volatile, and brief (Lane, Beedie, & Terry, 2007) and although they may be strictly related, they should be separated. Furthermore, the understating of emotions requires their operationalization and at least two positions on emotions' nature coexist, one hypothesizes the existence of a small number of basic emotions such as happiness, sadness, disgust, anger, fear, and surprise (e.g., Ekman et al., 1987). The second position comprises the dimensional theories that consider emotions as represented in an N-dimensional space where the two cardinal dimensions "valence" and "arousal" are extremely important (Russell & Barrett, 1999). Valence varies from negative, neutral, through positive values, whereas the arousal dimension refers to the intensity of emotions and varies from very low to very high (Viinikainen et al., 2010); the combinations of the levels of such dimensions could frame most of the emotional phenomena. However, social constructionists (e.g., Hochschild, 1979; Shott, 1979) argued that the number of emotions is indefinite, and might be rather defined and constructed by the societies; therefore, every "new"

emotion will play a functional role within a specific social system (see Averill, 1980), accordingly Kemper (1987) also stated that the number of emotions is constrained by the autonomic options. That is to say that the number of emotions is physiologically *finite*. The basilar assumption of social constructionists is that many emotions are deeply involved in social interactions (Scherer, Summerfield, & Wallbott, 1983) and, for instance, guilt is the result of the excessive use of power against someone else (Kemper, 1987). Shame, instead, occurs when individuals are discredited by their own actions (e.g., Izard, 1977); thus, guilt and shame differ with respect to their focus, in fact, while the first focuses on the acts that may have hurt someone, the latter is focused on the self and its status of unworthiness (Shott, 1979). More recently, Turner (2009, p. 341) supported the social nature of emotions suggesting that "it is true that emotions are channeled by culture and structural contexts, but the arousal of emotion itself is not a labeling process but, instead, a process by which body systems are activated to generate all emotions." Thereby, it sounds clear that emotions are a multifaceted construct that derives from the interaction of many different aspects. For the purpose of this work, it is worth it to understand how emotions can be linked to the immune system functioning. First, it has been hypothesized a physiological pathway (see Cole, 2008), as emotions are associated with the activation of the Autonomic Nervous System and more specifically positive and negative emotions have an opposite effect (cf. Kreibig, 2010). Anger, for instance, is associated with cardiovascular alteration caused by α and β-adrenoceptor (receptor of catecholamine such as epinephrine and norepinephrine). Danielson, Matheson and Anisman (2010), and Carroll et al. (2011), found also a relationship between anger and Il-6 that, however, was not supported by Moons, Eisenberger and Taylor (2009). Among the emotions that showed a peculiar physiological pattern, it should be mentioned "disgust," which is actually slightly more complex than other negative

emotions. In fact, it resulted characterized with two physiological patterns related to the stimulus that provoke the emotion, thus whether it is provoked by contamination (e.g. a dirty face) or mutilation (e.g. mutilation scene or bloody injuries). The former is characterized by increased heart rate, whereas the latter may show a decreased heart rate (cf. Kreibig, 2010); this difference may be seen in relation to a mental disorder highly correlated with disgust, namely the obsessive-compulsive disorder. In fact, in patients diagnosed with this disorder, disgust is accompanied by greater production of norepinephrine (Fluitman, Denys, Heijnen, & Westenberg, 2010), and although it is a very specific case, it may help to understand the physiological pattern of disgust. Furthermore, Buske-Kirschbaum, Geiben, Wermke, Pirke and Hellhammer (2001) documented an association between disgust provoked by contamination (e.g., dirty dishes), the activation of the herpes labialis and greater level of TNF-α , which was likely increased by the herpes labialis. Another emblematic example may be "hostility," which has been found to correlate with greater catecholamine (e.g., (Hughes, Sherwood, Blumenthal, Suarez, & Hinderliter, 2003), and TNF-α (Suarez, Lewis, & Kuhn, 2002). Notably, as Ricci Bitti, Gremigni, Bertolotti and Zotti (1995) pointed out, anger and hostility may be a risk factor for adverse cardiac events (cf. Gremigni & Ricci Bitti, 2000) and this is in line with the assumption about the role of emotions in stimulating catecholamine production. Psychoimmunological studies have also documented cytokines-related reaction linked to negative "social"-emotions such as shame, which Dickerson, Kemeny, Aziz, Kim and Fahey (2004) consider a "self-related" emotion that they found to correlate with TNF-α (see also Dickerson, Gable, Irwin, Aziz, & Kemeny, 2009). Brydon et al. (2009) also found that Il-6 production in reaction to vaccine injection is higher if patients were previously exposed to emotionally stressful events (e.g., public speech), and in conclusion, it should be noted that most of the negative emotions are

associated with greater cortisol (Buchanan, al'Absi, & Lovallo, 1999). Hence, the physiological patterns associated with negative emotions that have been illustrated may offer insights on how negative emotions may be connected to unfavorable health physiologically. On the other hand, positive emotions have showed a substantial opposite, respect to negative emotions, physiological activation. Jung and colleagues (2010), for instance, have observed that positive emotions are associated with dopamine (a neurotransmitters) in individuals attending a meditation group; furthermore, Brummett, Boyle, Kuhn, Siegler and Williams (2009) have found a relationship between positive emotions and reduced cardiovascular reactivity (cf. Kreibig, 2010), norepinephrine level, and awakening salivary cortisol. Happiness, indeed, has been quite frequently associated with lower risk of cardiac disease whereas stress increases it (Lane, Reis, Peterson, Zareba, & Moss, 2009). Interestingly, Burgdorf and Panksepp (2006) suggested a neuroanatomical substrates subdivision in the brain of positive emotions, depending on their arousal if low or high. In fact, high arousal positive emotions are "appetitive" and devoted to foraging, and reward seeking, whereas low arousal positive emotions are related to "pleasure" and more related to the consummation of reward. These two categories of positive emotions may show different autonomic nervous system patterns or cardiac changes (Stephens, Christie, & Friedman, 2010; Codispoti, Surcinelli, & Baldaro, 2008) as well as lower Il-6 (Doyle, Gentile, & Cohen, 2006; Janicki-Deverts, Cohen, Doyle, Turner, & Treanor, 2007; Prather, Marsland, Muldoon, & Manuck, 2007). Therefore, positive emotions could exert a protective effect on individuals' health physiologically. In fact, Aschbacher et al. (2011) have observed that during a stress task, participants who maintained a state of "positivity" were less likely to develop depression over time whereas, decline on positivity and the increased Il-1β, predicted the development of depression.

However, in most of the studies discussed so far it has been adopted a self-report "explicit" assessment of emotions, the regulation of HPA system may be rather automatic and does not need to be *consciously* recognized (e.g., LeDoux, 1996). For this reason, self-report and conscious emotions assessment may reflect many different things aside emotional experiences (Robinson & Clore, 2002) whereas implicit assessment of emotions could capture more appropriately the automatic process (Quirin, Kazén, Rohrmann, & Kuhl, 2009; cf. Fazio & Olson, 2003; Olson & Fazio, 2003). Nevertheless, implicit and explicit assessments of emotions may be correlated but, to some extent, still independent (Hofmann, Gawronski, Gschwendner, Le, & Schmitt, 2005); Quirin et al. (2009) claimed, indeed, that implicit emotions predict arousal of HPA better than the conscious self-reports do. Accordingly, the authors found implicit low positive emotions to predict, e.g., increased morning cortisol (Lai et al., 2005), whereas implicit negative emotions predicted acute cortisol responses to a stressor. Therefore, the assessment of emotions should comprise implicit and explicit measures, in order to have a wider understating of individuals' emotional experience.

The physiological pathway described above substantially reflects the mechanism that occur "under-the-skin" while it is not negligible that there is also an overt behavioral pathway to be considered. In fact, negative emotions could lead individuals to engage in unhealthy behavior such as alcohol use (Buchmann et al., 2010; Cooper, Frone, Russell, & Mudar, 1995), and Heatherton and Baumeister (1991) suggested that individuals might also engage in binge eating in order to distract oneself from emotional stress (Evers, Stok, & de Ridder, 2010). Positive emotions, instead, may promote more functional behaviors and could improve quality of sleep (Bardwell, Berry, Ancoli-Israel, & Dimsdale, 1999; Fosse, Stickgold, & Hobson, 2002), and engagement in healthy behaviors such as physical exercise (Ryff, Singer, & Dienberg

Love, 2004); notably, both examples have extremely beneficial effect on health (e.g., Cohen, Tyrrell, Russell, Jarvis, & Smith, 1993; Luoto, Prattala, Uutela, & Puska, 1998; Wingard, Berkman, & Brand, 1994). Accordingly, Smith and Baum (2003) have suggestively hypothesized that positive emotions encourage restorative activities such as sleep, exercise, relaxation, which in turn act buffering the appraisal of stress, and therefore, emotions may be influential at least on two levels.

1.6 Personality

The construct of personality has been defined as a stable and consistent pattern of emotions, cognitions, and behaviors that characterize individuals and are involved in determining individuals' health, principally through behaviors. The most used model that explains individuals difference on the basis of five main dimensions, has been developed by Costa and McCrae (1995; McCrae & Costa, 1987; Goldberg, 1990) who have identified five main dimensions (each composed of two facets), namely the Big Five model. More precisely, these dimensions are Neuroticism (N), Extraversion (E), Openness to Experience (O), Agreeableness (A), and Conscientiousness (C), which have been thought to underlie two second order dimensions, Plasticity and Stability (DeYoung, 2006; Musek, 2007). Conscientiousness and neuroticism have showed the strongest association with health outcomes (Hampson & Friedman, 2008), the individuals who are low in conscientiousness tend to be disorganized, irresponsible, and undisciplined, and are very likely to engage in behaviors such as smoking, drinking, and deregulated diet (Friedman et al., 1993; Hampson, Goldberg, Vogt, & Dubanoski, 2007; Roberts, Kuncel, Shiner, Caspi, & Goldberg, 2007). They are also at greater risk to suffer from, e.g., diabetes, hypertension, urinary problems, stroke and a variety of mental illnesses, and not least earlier mortality (Bogg & Roberts, 2004;

Roberts & Bogg, 2004; Raynor & Levine, 2009). Likewise those who are high on neuroticism are characterized with "negative emotionality" (Watson & Tellegen, 1985; McCrae & Costa, 1987) and greater difficulties to cope with and control negative emotions (e.g., irritation, discontent, and anger). For this negative emotional arousal, neuroticism may promote an overreaction to stress and amplify the negative consequences of the exposure to stress (Bolger & Schilling, 1991; Kling, Ryff, Love, & Essex, 2003; Mroczek & Almeida, 2004). High neuroticism is, indeed, associated with greater plasma cortisol (Miller, Cohen, Rabin, Skoner, & Doyle, 1999), and particularly with the awakening time cortisol peak (Phillips, Carroll, Burns, & Drayson, 2005; Portella, Harmer, Flint, Cowen, & Goodwin, 2005). Interestingly, both neuroticism and low conscientiousness correlate with Il-6 production (Sutin et al., 2010), and may promote greater systemic inflammation. Hence, certain personality traits may act on health through two pathways as argued by Turiano and colleagues (2012), who also suggested that hostility facet of agreeableness might predict poorer health outcomes (see also Brummett et al., 2006). Agreeableness is the personality trait characterized with high interpersonal attitudes and behaviors (Costa & McCrae, 1992), whereas on its negative pole it reflects the "cynical hostility" (Friedman, Tucker, & Reise, 1995). Thus, individuals low in agreeableness may tend to experience greater neuroendocrine activation in response to psychological stress (cf. Suarez, Kuhn, Schanberg, Williams, & Zimmermann, 1998) and greater blood pressure, epinephrine, norepinephrine, and cortisol (Miller et al., 1999; Pope & Smith, 1991; Suarez & Blumenthal, 1991). Contrariwise, high level of agreeableness might buffer the stress reaction (e.g., lower epinephrine) after a speech in front of an audience (Wirtz, Siegrist, Rimmele, & Ehlert, 2008), and could also exert a protective effect on physical health as supported by the studies that showed individuals high on agreeableness are less likely to develop common cold symptoms after the exposition

to a virus (Cohen, Doyle, Turner, Alper, & Skoner, 2003). This suggests that agreeableness can be directly or indirectly associated with the immune system functioning, as also extraversion might be (Cohen et al., 2003); in fact, such a trait, strongly characterized with the preference for social interactions and more positive affect (Costa & McCrae, 1992), characterizes individuals that are more optimism and this may lead to a more positive health (Danner, Snowdon, & Friesen, 2001). On the other hand, the opposite facet of extraversion, "*introversion,"* is characterized with higher sensitivity to rejection, namely the degree to which one expects and perceives negative evaluations and social refuse. Introversion can be associated with higher systolic blood pressure, diastolic blood pressure, epinephrine, and norepinephrine (Miller et al., 1999) and might ultimately predict earlier mortality (e.g., Danner, Snowdon, & Friesen, 2001). Lastly, the relationship between openness and health has been less investigated; yet, Hampson and Friedman (2008) found higher levels of openness to be protective against earlier mortality. Moreover, Duberstein et al. (2003) argued that openness is highly correlated with happiness, positive affect, and quality of life, which could promote the process of salutogenesis. Taken together, personality traits (namely, their facets) associated with healthy behaviors, positive emotions, and reduced stress reaction, could exert a protective effect on individuals' health. Whereas, on the other hand, personality traits, or their facets, which are associated with unhealthy behaviors, negative emotions, and amplified reaction to stress might represent risk factors instead.

1.7 Alexithymia

The term a-lexi-thymia refers to the deficit in understanding, processing, or describing emotions (Nemiah, Freyberger, & Sifneos, 1976; Taylor, Parker, & Bagby,

1999), in fact, the word is composed by the *alpha* privative and the Greek words *lexis* "diction, word," and *thumos* "soul, as the seat of emotion, feeling, and thought." Thereby, alexithymia literally means "without words for emotions," and exactly describes the features of this cognitive deficit. The alexithymic individuals, in fact, are characterized with a significantly reduced or total absent emotional experience together with an impaired awareness about emotions (Taylor, Bagby, & Parker, 1999). Nevertheless, they may be still able to elaborate the emotional information implicitly, ultimately failing in reporting them explicitly (Lane, Ahern, Schwartz, & Kaszniak, 1997; see also Köhler & Moscovitch, 1997) and the behavioral and autonomic responses generated by the implicit process of emotional stimuli might still occur due to the emotional arousal (Lane et al., 1997). For the difficulty in reporting their emotion in words, alexithymic individuals might be expected to self-report lower positive and negative emotions, whereas they generally self-reported greater negative emotions and lower positive emotions (Lumley, Mader, Gramzow, & Papineau, 1996; Palmer, Donaldson, & Stough, 2002), which might be due to the unprocessed emotional arousal.

The researchers who have investigated the construct of alexithymia have also discussed whether it should be considered a trait or a state Bagby, Taylor and Parker (1994), for instance, have considered alexithymia as tightly associated with certain personality traits of the Big Five model, namely they argued it to substantially overlap “openness to experience” (Costa & McCrae, 1992), and to be associated with neuroticism, as alexithymic individuals tend to experience negative emotions. Jessimer and Markham (1997) claimed that alexithymia is a personality trait in line with Salminen, Saarijärvi, Toikka, Kauhanen, and Äärelä (2006) who also found the construct to be stable over five years. Furthermore, Becerra, Amos, and Jongenelis

(2002) introduced the term “organic alexithymia” that refers to the cognitive deficit occurred after a brain injury taken together, then, alexithymia may be thought as a rather stable characteristic that can have a neurobiological origin, and that is quite recurrently associated with psychosomatic illness (e.g., Taylor, Bagby, & Parker, 1991). Martin and Pihl (1985), in fact, have hypothesized that alexithymia confers greater vulnerability to stress magnifying the reaction to stress with a consequent increased level of cortisol (de Timary, Roy, Luminet, Fillée, & Mikolajczak, 2008; Franz et al., 1999). This increased vulnerability might derive by the “anticipatory” feature of alexithymia (de Timary et al., 2008) since individuals could overreact to stressors expecting them to be *stressful*. This may also explain the greater inflammation, and greater level of Il-6 and TNF-α observed in alexithymic individuals (Bruni et al., 2006; Honkalampi et al., 2011; Temoshok et al., 2008), together with the unhealthy behaviors associated, such as alcohol (Hendryx, Haviland, & Shaw, 1991) and substance abuse (Lindsay & Ciarrochi, 2009). Hence, similarly to the constructs described above, alexithymia may affect health through two parallel pathways.

One major issue related to alexithymia is related to the psychometric instruments available (e.g., Bermond–Vorst alexithymia questionnaire by Vorst & Bermond, 2001; Observer Alexithymia Scale by Haviland, Louise Warren, & Riggs, 2000), of which the most popular and widely used one is the Toronto Alexithymia Scale (TAS-20; Bagby et al., 1994). This instrument is composed of three dimensions: difficulties in identifying feelings (DIF), difficulties in describing feelings (DDF), and externally oriented thinking or a preoccupation with the details of external events (EOT). While the subscales DIF and DDF are generally highly correlated, the EOT subscale may be poorly correlated and not sufficiently reliable (e.g., de Timary et al., 2008; Parker,

Taylor, & Bagby, 2003; Säkkinen, Kaltiala-Heino, Ranta, Haataja, & Joukamaa, 2007). Furthermore, alexithymia might exhaustively captured by the DIF rather than by DDF and EOT subscales (Haviland, Shaw, Cummings, & MacMurray, 1988). Nevertheless, DIF and DDF are both extremely important since they are associated with psychopathological conditions (e.g., Carré et al., 2011; Evren et al., 2008; Hendryx et al., 1991; Rose & Segrist, 2012); thus, while it may be debatable the use of an overall score or of the diagnostic clusters, there is no doubt about the effect of the single dimensions on health outcomes.

1.8 Perceived stress: The importance of the cognitive appraisal

In the paragraph § 1.2, we have introduced the construct of stress and its deleterious effects on health; however, it is worth to make a distinction between objective and subjective components of stress. In fact, certain events may be objectively stressful, such as bereavement (W. Stroebe, M. S. Stroebe, K. J. Gergen, & M. Gergen, 1982) whereas others might be *perceived* as stressful, that is, they are stressful to the extent to which they are cognitively evaluated as such (e.g., Lazarus, 1966). Cohen, Kamarck, and Mermelstein (1983), in fact, have claimed that the assessment of objective stress caused by, e.g., unemployment, may be limited and not fully informative (Dooley & Catalano, 1980; Gore, 1978). Additionally, life-event scale (e.g., Holmes & Rahe, 1967) that provides a cumulative score of stress (e.g., B. P. Dohrenwend & B. S. Dohrenwend, 1981), does not assess perceived stress, which may be seen as an "outcome," or a result of the mutual interaction of individuals' resources with the stressors one is facing with. In line with the general adaption syndrome, indeed, stressful events may lead to an acute reaction, followed by the resistance stage, and individuals' resources largely determine the eventual transition to the stage of

exhaustion (cf. Selye, 1950). Therefore, as affirmed by Boals and Banks (2012), the concept of stress itself refers to the individuals' perception that an event is unpredictable, uncontrollable, and overloading; therefore, perceived stress is a commingling of factors such as the occurrence of objective stressors, the coping strategies adopted, the individuals' personality traits, and their resources (Cohen et al., 1983). Taken together, then, the appraisal of events as stressful is a fundamental process, in line with Lazarus and Folkman (1984a, 1984b) who described the person-environment transactions as a dynamic, mutually reciprocal, bidirectional relationship, which must be considered along with the appraisal of the stressors and the social and cultural resources available (Samson & Siam, 2008; Antonovsky & Kats, 1967). The two processes included in this model are the cognitive appraisal and coping, which both act as mediators of the relationships between the person and the environment (Lazarus & Folkman, 1984a, 1984b). Thereby, the cognitive appraisal of events starts with the evaluation of the threat of a stressor; then, as a second step, individuals establish whether they can act to face or prevent the threat that derives from the stressors. In other words, the stressors that threaten one's health or stability, and that are subjectively perceived as sources of stress, may increase stress perception. Stressors can be distal or proximal either on a temporal dimension (e.g., Ensel & Lin, 1996) and/or in relation to their virtual position and distance from individuals' self (see Meyer, 1995, 2003); this "ambiguity" about stressors' definition as distal and proximal, may cause confusion and needs to be more further addressed. (B. S. Dohrenwend, 1978, p. 3) stated "[…] stressful life events vary to the extent to which they are determined by the environment or by psychological characteristics of the central person in the event". This may provide support to Meyer's (2003) definition of distal and proximal stressors based on their position respect to the individuals' self, although the stressors might be considered distal or

proximal with respect to their position within the system in which individuals live. That is to say, stressors may be placed on a continuum that describes the social levels, namely the individual level, the inter-individual (e.g., dyadic), or groups level, through the higher system of, e.g., culture or law (cf. Bronfenbrenner, 1977a, 1977b). Exemplifying what has been said, stressors may be related to individuals directly (e.g., the diagnosis of HIV) or could derive from the relationships in which individuals are directly involved (e.g., doctor-patient). Likewise, stressors can be linked to the relationships in which one is *indirectly* involved (e.g., patient-doctor-hospital) or, lastly, stressors may also derive from the society (e.g., stigma associated with HIV). Accordingly, Herek (2011) referred to sexual stigma that affects gay and bisexual individuals and described the structural social stigma, namely the one deriving from social processes. Interestingly, despite the great variety of stressors (e.g., distal/proximal, or psychosocial, and biological) the physiological reaction to them may be still very similar; in fact, the consequences may be very similar independently from the nature of the stressors, which may produce the shortening of the telomere (Epel, 2009; Epel et al., 2004), increased level of cortisol (e.g., Ebrecht et al., 2004; Pruessner, Hellhammer, & Kirschbaum, 1999), or also greater Il-6 (Cohen, Doyle, & Skoner, 1999; Kiecolt-Glaser et al., 2003). As a result, greater inflammation and severe impairment of the immune system might occur (e.g., Akbar & Vukmanovic-Stejic, 2007).

Perceived stress can also act through behaviorally by increasing the rates of unhealthy behaviors such as less frequent exercise, cigarette smoking, a higher fat diet (Ng & Jeffery, 2003), and the emotional eating (Sims et al., 2008); consequently, perceived stress as well, acts on two levels the behavioral and the physiological one and both might contribute to worsen individuals' health status.

1.9 Minority stress: A psychosocial form of stress

A construct strictly linked to perceive stress is that of minority stress, which was introduced and extensively described by Meyer (1995, 2003) who strenuously claimed that the members of minority groups, such as gay and bisexual men, are at risk for mental health, due to a specific form of social stress. Such a stress is, indeed, generated by the existence of a conflict between the members of minority groups and the society they live in (e.g., Lazarus & Folkman, 1984a, 1984b); since a harmonious relationship is fundamental for a healthy living (e.g., Selye, 1993), such social conflicts increase stress (Meyer, 2003). More specifically, the stigma associated with the belonging to a minority group, could expose the members of minority groups to an additive social stress generated by the "minority stressors," namely the stigma manifestations (see Meyer, 1995, 2003). Minority stress is thought to be chronic, since it is generated by stable processes either social or cultural; furthermore, its effect adds to "general stress," which is instead experienced by members of non-stigmatized groups as well. On one hand, minority stress is added to general stress with a consequent increased vulnerability for the members of minority groups, to mental and physical disorders (Meyer, 1995, 2003). Four minority stressors have been initially defined by Meyer (1995, 2003) and, in a second time, Herek (2009, 2011) introduced the structural stressors. All these stressors can be placed on an ideal continuum that goes from *distal* through *proximal* with respect to the individual's self (Meyer, 1995, 2003; § 1.8). The first and more distal stressor is "enacted sexual stigma," which refers to the physical or verbal manifestations of stigma such as homophobic hate crimes towards gay and bisexual individuals. On a more proximal position, there is a stressor denominated "expectations of discrimination," which is the individuals' expectations to be treated unfairly and/or unequally respect to members of non-stigmatized groups. Such expectations might be reinforced by the

perception of hostility from the social environment generated by social and legal reactions, or the lack of reactions, to homophobic hate crimes (Herek, 2004, 2009; Meyer, 1995). Likewise, the individuals who have been victimized because of their sexual orientation could also expect that future discriminations might occur (Kelleher, 2009), consequently they could feel the need to keep high level of vigilance that will eventually promote stress (Meyer, 1995). The third source of minority stress is the "concealment of one's sexual orientation," a sort of self-protective strategy enacted to prevent discrimination or hate crimes (Meyer, 2003). Individuals have to use great efforts and resources to keep their sexual orientation "hidden," and this could lead to exhaustion, and chronic (minority) stress. The fourth stressor refers to the introjection of the sexual stigma by gay and bisexual persons, who direct homophobic attitudes towards oneself (Herek, 2004; Meyer, 2003). This is the so-called "internalized homophobia" that undoubtedly generates psychological distress due to the intrapsychic conflicts linked to relationship with individuals' self. Meyer (2003), in fact, considered it as the most insidious and proximal (to the self) source of minority stress (cf. Meyer & Dean, 1998). The "structural minority stressor" described by Herek (2011), instead, consists in social process-based stressors, which essentially convey societal stigma towards gay and bisexual individuals. Accordingly, the absence of legal rights for same-sex couples could reinforce the perception of societal heterosexism; albeit social and legal rights are "objective," it should be not given for granted that all individuals would perceive them as stressors. For instance, there may be individuals who do not feel discriminated for the lack of the same-sex marriage since they do not want to get married. Thus, the appraisal might be more informative, in line with the subjective appraisal of stressors. Lastly, a distinction between discrimination and prejudice should be also done; although within the literature about minority stress it has been not addressed, it could be assumed that

the expectations to be stereotypically defined as pedophilic, perverted, and abnormal persons because of the sexual orientation would cause stress (see Boysen, Vogel, Madon, & Wester, 2006; Herek, 1991; King, 2004). Thereby, the stressors described above may cause an additional load of stress caused by minority stressors that could increase the risk of mental disorders (Meyer, 1995, 2003) directly, and indirectly by increasing perceived stress (Schwartz & Meyer, 2010; cf. Pascoe & Smart Richman, 2009). The stressors might act causing a physiological dysregulation (e.g., greater cortisol), the same consequences as those cited for stress and perceived stress (see § 1.8) with risk of impairment on the functioning of the immune system (e.g., Wüst, Federenko, Hellhammer, & Kirschbaum, 2000). Furthermore, minority stress might also promote the adoption of unhealthy behaviors such as alcohol and substance abuse (Hatzenbuehler, Nolen-Hoeksema, & Erickson, 2008; Lehavot & Simoni, 2011), suggesting that the members of a minority group can be at greater risk for their health.

1.10 Depression

Depression is the most common mental disorder that currently affects about 350 million of people worldwide (http://www.who.int/mediacentre/factsheets/fs369/en/index.html), and it is expected to cause great disability in the general population (Davidson & Meltzer-Brody, 1999). In fact, together with a greater impairment of the quality of life (e.g., social, and work), depression might ultimately lead to suicide (Rihmer & Gonda, 2012); therefore, depression should be routinely assessed in health care contexts, especially in patients with chronic illness as they are at greater risk for depression (Clarke & Currie, 2009; Rabkin, 2008). Depressed individuals may show a range of

psychological and physical symptoms (DSM-IV-tr, APA, 2000) such as depressed mood for most of the day and nearly every day, anaehdonia (namely, markedly diminished interest or pleasure in all, or almost all activities). Furthermore, individuals could show decreased or increased appetite and insomnia or hypersomnia quite every day. Someone may exhibit psychomotor agitation or retardation, fatigue or loss of energy, feelings of worthlessness or excessive/inappropriate guilt. Moreover, depressed individuals might show impaired ability to think or to concentrate, greater indecisiveness and recurrent thoughts of death, as well as suicidal ideation or a suicide attempt. The World Health Organization (WHO, 2012a, 2012b) recently provided a report on mental health in which it has been found the risk for depression to be higher for women than men (WHO, 2008). Besides, economic and social disadvantages, genetics, exposure to violence, being separated or divorced, and chronic illnesses are all risk factors for depression (WHO, 2012a, 2012b). The physiological changes and behavioral patterns associated with depression could explain why it is extremely harmful for the health; in fact, it has been observed greater cortisol as well as pro-inflammatory cytokines (Zunszain et al., 2011), and the immune system may be consequently impaired, e.g., for the lower natural killer[1] (Steel, Geller, Gamblin, Olek, & Carr, 2007). Accordingly, Evans et al. (2008) found that the administration of antidepressant (SSRI; Selective Serotonin Reuptake Inhibitors) was accompanied by improved immunity and greater natural killer counts, likewise the neurotransmitter serotonin is associated with the process of phagocytosis[2] and with chemokines[3] production in macrophages (Mikulski et al., 2010; Nakamura, Sato, Ohashi, Tsurui, & Hasegawa, 2008). Furthermore, Yin,

[1] Natural Killer (NK) are lymphocytes cells of the innate immune system.

[2] Phagocytosis is process through which bacteria or viruses are literally engulfed and digested by immune cells.

[3] Chemokines are a family of small cytokines.

Albert, Tretiakova, and Jameson (2006), and Inoue et al. (2011) observed that the level of serotonin was correlated with the T cell proliferation hence, such physiological associations may explain why depression could cause major harms in patients' well-being. On the other hand, depression and impaired immunity could be both the consequences of greater inflammation and the activation of the IDO enzyme that may contribute in lowering serotonin (caused by the depletion of tryptophan) and increasing kynurenine (the tryptophan metabolite), which has proven to reduce T-cell reactivity (Fallarino et al., 2003). The co-occurrence of depression and impaired immunity, then, might be also seen as the consequence of greater inflammation. As discussed above, emotions and mood differ but are associated, for instance, the symptoms of depression include excessive or inappropriate guilt (APA, 2000). Furthermore, it may be also observed greater hostility, less control on anger (Biaggio & William, 1987; Fava et al., 1993), worry (Borkovec, Wilkinson, Folensbee, & Lerman, 1983) and shame (Andrews, Qian, & Valentine, 2002). Given the association of emotions with inflammation and the immune system functioning, the increased negative emotions could amplify the negative effect of depression on health. Likewise, the behavioral correlates of depression can be undoubtedly influential since depressed individuals may abuse of alcohol (Conner, Pinquart, & Gamble, 2009), and they may show inadequate self-care as observed in patients underwent transplant (e.g., Cukor, Rosenthal, Jindal, Brown, & Kimmel, 2009), and HIV-positive patients (Rabkin, 2008).

1.11 Positive thinking

Scheier and Carver (1993) have initially considered positive thinking as the general expectancies that good things will happen in one's life, namely the construct of

optimism; however, Caprara et al. (2009) have recently broadened the concept of positive thinking referring to an "optimal functioning syndrome" and claiming that it may act as a protective factor against mental illness and against depression in particular (Steca & Caprara, 2007). The authors conceived positive thinking to be composed by self-esteem, optimism, and life satisfaction (Caprara, Steca, Gerbino, Paciello, & Vecchio, 2006), the more important components of individuals' well-being (Carver & Scheier, 2002; Kahneman, Diener, & Schwarz, 2003). The dimension of self-esteem refers to the individual global regard and acceptance for oneself as a person (Harter, 1993), whereas optimism, in line with Scheier and Carver (1993), was operationalized as one's expectations that the future holds good things and life satisfaction corresponds to the evaluation of life satisfaction in accord with individuals' standards (see Caprara et al., 2006). Each factor, have been individually associated with lower risk for anxiety and depression (Baumeister, 1993; Greenberg et al., 1992), instance, then, individuals with moderately high self-esteem may engage in more efficacious strategies to achieve their goals (Kernis, 1995); furthermore, they may also feel to be capable to exert control over life events (Tedeschi & Norman, 1985). Optimism, instead, has been associated with better physical health and greater longevity (Carver & Scheier, 2001; Carver & Scheier, 2002; Maruta, Colligan, Malinchoc, & Offord, 2000); moreover, optimistic individuals tend to adopt more functional coping strategies, especially in case of serious illness (e.g., Ben-Zur, Rappaport, Ammar, & Uretzky, 2000). Finally, life satisfaction may be associated with lower risk of depressive symptoms over the time (Koivumaa-Honkanen, Kaprio, Honkanen, Viinamäki, & Koskenvuo, 2004). These constructs are also linked to more favorable physiological changes, such as lower Il-6 for optimism (Brydon, Walker, Wawrzyniak, Chart, & Steptoe, 2009), and greater NK counts for life satisfaction (Tsuboi et al., 2005).

1.12 Adherence and compliance: The emerging construct of adherence perceived self-efficacy

Chronic illness requires daily self-care and patients should be "adherent" with behavioral, and pharmacological prescriptions as well as with medical appointments in order to improve their health status. The patients are, indeed, directly involved in their therapeutic process; they must be active in the illness management with perseverance and regularity in following the prescriptions, which largely determines patients' health outcomes. In the literature about health psychology, a fundamental distinction between the two concepts of adherence and compliance, which sometimes have been used as synonymous, has been provided. In fact, while compliance refers to the extent to which individuals take the pills prescribed, adherence rather refers to a wider range of illness-related behaviors (e.g., the regularity of medical visits). These concepts are quite intuitively related where compliance may be considered part of adherence, and both ensure better clinical outcomes especially in chronic diseases (DiMatteo, Giordani, Lepper, & Croghan, 2002). However, the relationship between adherence and health might be more complex than it can be assumed (Hays et al., 1994). Chronic illness, in fact, requires major adjustments in one's life, and individuals may face a variety of stressful circumstances involving a range of adaptational demands (Burish & Bradley, 1983). For instance, patients might have to cope with the threat of the disease progression, and with the challenge of modifying their behavior to meet the demands of a prescribed treatment regimen. Patients, then, should perceive themselves as capable to succeed in such an adaptation process (Meichenbaum & Turk, 1987) and, more precisely, the perceived self-efficacy may play a decisive role. Individuals should perceive to possess the ability to enact the behavior required as in the case of adherence and this would promote a better clinical outcome as demonstrated in hypertensive (Ogedegbe, Mancuso, Allegrante, &

Charlson, 2003), and diabetic patients (Littlefield et al., 1992) as well as in HIV-positive individuals (Johnson et al., 2007). Hence, greater perceived self-efficacy may be associated with more favorable clinical outcome (e.g., Bandura, 1989; Bangsberg et al., 2006; Johnson et al., 2007; Paterson et al., 2000), as well as lower risk of depression (Bandura, 1989). Since depression has proven to reduce adherence in chronic illness (Grenard et al., 2011) and in HIV-positive individuals in particular (Bhatia, Hartman, Kallen, Graham, & Giordano, 2011; Kroenke, Spitzer, & Williams, 2001; Halkitis, Parsons, Wolitski, & Remien, 2003), perceived self-efficacy related to adherence might also act indirectly on physical health by reducing depression and enhancing adherence to medication.

1.13 Illness perceptions: How patients represent their illness

There is evidence that individuals affected by the same illness may react differently and cope with illness engaging in diverse behaviors likely guided by the perceptions they have of their disease. While there are certain objective aspects (e.g., hair loss caused by chemotherapy), some others may be more subjectively perceived (e.g., influence on one's emotions) and therefore, in line with the self-regulation model (Leventhal & Diefenbach, 1991), patients may build a representation of their illness, which in turn could determine the coping strategies they adopt. Such a representation is based on specific features such as the identity, the cause, the time-line, and the consequences of the illness. (Lau, Bernard, & Hartman, 1989) incorporated also the beliefs about the cure and controllability of one's condition, whereas Kaptein (2007) and Broadbent (2007) introduced the aspect of coherence. The *identity* refers to the patients' thoughts about, e.g., the label and the nature of their condition; the *cause* consists in the patients' beliefs about "what caused their condition," where the *time-*

line is the patients' perceptions of their illness duration (e.g., acute/chronic). The dimension of *consequences* reflects, instead, the patients' beliefs about illness severity while the *cure* is related to the beliefs about the therapy and the control that patients exert over it and the *coherence* reflects how well the patients understand their illness and lastly. Furthermore, Leventhal, Nerenz, and Steele (1984) proposed that the emotional responses are processed in parallel to illness representations; therefore, the illness emotional component should be included as well (see Broadbent, Petrie, Main, & Weinman, 2006). All of these aspects are distinct and correlated at the same time, and may interact in determining patients' behavior, for instance, e.g., greater control may be linked to better adherence (Griva, Myers, & Newman, 2000; Senior, Marteau, Weinman, & Group, 2004). Illness perception is associated with depression (Murphy, Dickens, Creed, & Bernstein, 1999), in fact, as claimed by Sharpe, Sensky, and Allard (2001), illness perception together with coping strategies may predict the development of depression over time and, the assessment of illness perceptions, might be useful to predict patients' reaction (see also Sacks, Peterson, & Kimmel, 1990). In patients suffering from arthritis, illness perception mediated the association between the physical symptoms and passive coping (Zyrianova, Kelly, Sheehan, McCarthy, & Dinan, 2011) and, likewise, as demonstrated in patients with Parkinson, illness perception was associated with anxiety and depression, and dysfunctional coping mediated the relationship between illness perception and mental health (Evans & Norman, 2009). Additionally, an intervention aimed to modify patients' illness perception produced an improvement on coherence and control, and enhanced the rates of return to work in patients who suffered from myocardial infarction (Broadbent, Ellis, Thomas, Gamble, & Petrie, 2009). Hence, the modification of the various facets of illness perception may promote a better adjustment to chronic illness. Furthermore, the emotions related to illness perception

might be also linked to a worse adherence if mediated by medication concerns (Nicklas, Dunbar, & Wild, 2009); however, the perception of control seems to be the most influential aspect enhancing the adherence to medication (Chen, Tsai, & Chou, 2011; Petrie, Perry, Broadbent, & Weinman, 2011). Taken together illness perception is extremely relevant in the context of health care either for its effect on mental health as well as coping strategies, which resulted extremely significant as well and deserve to be further addressed.

1.14 Coping

To fully understand the concept of coping it is necessary to refer to the model of "stress and coping" (Lazarus & Folkman, 1984a, 1984b) in which it is stated that stress and emotions are products of the cognition, and once aroused, emotions might also affect cognition through a circular relationship. The Author underlined the fallacy of adopting the Stimulus-Response perspective to understand the link between stress and performance, and introduced the role of the individual differences in such a relationship. Under the condition of stress, three possible responses might occur: 1) no measurable effect, 2) impairment of performance, 3) facilitation (Lazarus & Folkman, 1984a, 1984b). Thereby, coping may be defined as the cognitive and behavioral responses enacted by the individuals who face stressful events. Initially, Folkman and Lazarus (1984a, 1984b) have proposed two coping strategies: the problem-focused and emotion-focused; in the first one, individuals try to deal with the problem by removing the cause of stress, whereas in the second one they try to act on oneself modulating the emotional distress (see Monaci & Ricci Bitti, 1998). Carver and Connor-Smith (2010), however, claimed that there are many ways to cope with stress and, together with problem and emotion focused strategies, they included

engagement/disengagement to distinguish coping aimed to deal with stressors from coping aimed to avoid/escape the threat or the related emotions (e.g., Moos & Schaefer, 1993; Roth & Cohen, 1986; Skinner, Edge, Altman, & Sherwood, 2003). Engagement coping includes problem-focused coping and some forms of emotion-focused coping such as support seeking, emotion regulation, acceptance, and cognitive restructuring whereas disengagement coping (which is quite often emotion-focused) includes responses such as avoidance, denial, and wishful thinking. Furthermore, accommodative coping (or secondary-control coping; see also Morling & Evered, 2006; Skinner et al., 2003) refers to adjustments made in response to stressors and comprises responses such as acceptance, cognitive restructuring, and scaling back one's goals in the face of insurmountable interference. The meaning focused coping (see Folkman, 2008; Park & Folkman 1997) refers to the finding or reminding to oneself about the benefits of stressful experiences (Tennen & Affleck, 2002) and includes reordering life priorities and infusing ordinary events with positive meaning. This strategy is connected to the influence of positive feelings on outcomes, particularly for the individuals who try to find benefits and a meaning in adversities (Helgeson, Reynolds, & Tomich, 2006) and involves the process of reappraisal (Folkman, 2008). Lastly, as pointed out by Aspinwall and Taylor (1997), some coping strategies may occur proactively, that is, before the occurrence of any stressor as they are aimed to prevent threatening or harmful situations from happening. Coping strategies may determine the physiological reaction to stress; O'Donnell, Badrick, Kumari, and Steptoe (2008), for instance, found that "seeking social support" and "engagement coping" were associated with lower daily cortisol maybe as a consequence of the buffering effect of social support (see § 1.15). Bento et al. (2010) found that in women, but not in men, the perceived control mediates the relationship between active coping and cortisol level that may be the consequence of

a reduction in the perception of events' stressfulness (cf. Boals & Banks, 2012). The emotional coping strategy "emotional expression" and "emotional processing," are associated with better health outcome, e.g., among individuals with diabetes (Smalls et al., 2012). Dysfunctional coping, instead, is associated with poorest health outcome as claimed by Gonzalez, Mimiaga, Israel, Andres Bedoya, and Safren (2012), who found the individuals who coped with stress by using substances reported poorest adherence with ART. Likewise, Pence et al. (2008) observed that in HIV-positive individuals, the adoption of maladaptive coping (e.g., avoidance) was associated with alcohol use. Thereby, the influence of coping on health outcomes might be mediated by reduced stress reaction (e.g., cortisol) and with functional coping engaged to deal with the causes of stress.

1.15 The illness-related social support

Human beings naturally develop social attachment (e.g., Ainsworth, 1989) that plays an important part in psychological adjustment and health; social support, in fact, is "[…] denned as the existence or availability of people on whom we can rely, people who let us know that they care about, value, and love us" (Sarason, Levine, Basham, & Sarason, 1983, p. 127; cf. also Levine, Basham, & Sarason, 1983). Social support may promote a positive social context for individuals (Bettschart, Bolognini, Plancherel, Nunez, & Leidi, 1992) and could buffer the impact of stress (Plancherel, Bolognini, & Nunez, 1994; Roos & Cohen, 1987). It is a multifaceted concept and differs from "social interaction," which is rather related to the quantity of the social interactions whereas social support may reflect the perception of support (Shinn, Lehmann, & Wong, 2010). It has been argued that the beneficial effects of social support could be influenced by the source of stress, and for instance, patients suffering from a

stigmatized illness may be less likely to seek social support, unless they disclose or have already disclosed their condition. Furthermore, social support may be *perceived* and *received*, and the two aspects are not interchangeable (Wills & Shinar, 2000) since perceived support is subjectively evaluated and "potential." In other words, individuals know/perceive that they can count on social support, whereas received support is quantifiable and it is anchored to specific periods of life (e.g., Dunkel-Schetter & Bennett, 1990). These aspects are not necessarily correlated and perceived support may be beneficial even if it does not turn into actual support (Cohen & Syme, 1985; Cohen & Wills, 1985; see also Wills & Shinar, 2000), as claimed by Uchino (2006) that suggested *perceived* support be more likely associated with better health outcomes than the received support. However, interpersonal relationships have an overall protective effect on individuals' health (e.g., Kiecolt-Glaser, McGuire, Robles, & Glaser, 2002a, 2002b; Kiecolt-Glaser and Newton, 2001) since, for instance, social integration is associated with lower IL-6 and CRP C-Reactive protein (a non-specific index of inflammation) in older men (Ford, Vernon, Havstad, Thomas, & Davis, 2006; Loucks et al., 2006). Likewise, among socially isolated individuals, it has been observed a diminished regulation of leukocyte trafficking by cortisol in comparison to individuals who were more socially integrated (Cole, 2008). Furthermore, social support, which may be a consequence of social integration, positively acts on health as documented in pregnant women that showed lower CRP associate with greater social support (Coussons-Read, Okun, & Nettles, 2007). Additionally, women satisfied with their social relationships have showed lower IL-6 (Friedman et al., 2005) even if they were affected by ovarian cancer (Costanzo et al., 2005). It has been well-established that there are at least three types of social support, namely (1) emotional (providing caring, love and empathy), (2) instrumental (referred to by many as a tangible support), and (3) informative (e.g., guidance or feedback that

can provide a solution to a problem); they all can come from different sources such as the intimate partner, friends, and/or family (Heitzmann & Kaplan, 1988; Provost, 1995). Bolger and Amarel (2007) suggested that it is rather unlikely that different forms of support act in the same way to promote health, but they might act on several levels instead leading to lower reactivity to stress (e.g., Cohen & Wills, 1985; House, Landis, & Umberson, 1988) and cortisol level (Eisenberger, Taylor, Gable, Hilmert, & Lieberman, 2007). Accordingly, Bolger and Amarel (2007) found that emotional social support moderates the reactivity to stressors, however the authors found that this may happen only when the support was given without recipients' awareness. That is, when recipients were not aware to receive support that the authors called "invisible support." Additionally, Zhou et al. (2010) observed that in patients with prostate cancer, social support exerts a protective effect on emotional well-being mediated, in part, by adaptive coping. Social support has been also linked to emotions as discussed by Onoda et al. (2009) who observed an enhanced prefrontal cortex activity during emotional support; the authors concluded that social support might moderate the emotional response during a social exclusion task. Furthermore, there may be a behavioral pathway through which social support acts (DiMatteo et al., 2002) improving, for instance, adherence in heart failure (Sayers, Riegel, Pawlowski, Coyne, & Samaha, 2008), in breast cancer (Kroenke, Kubzansky, Schernhammer, Holmes, & Kawachi, 2006) and HIV-positive individuals (e.g., Ncama et al., 2008). Thereby, social support may be a precious resource for patients who have to deal with a chronic illness, and its action might be observed physiologically as well as behaviorally.

2. HIV/AIDS: Epidemiology, physiological mechanisms, and psychosocial components

In this chapter, a general introduction to HIV/AIDS illness and its physio-psychological consequences will be provided. Throughout the paragraphs, several aspects about HIV infection will be discussed, starting from the epidemiologic data that together with behavioral studies help to identify the individuals at greater risk to contract HIV. Then, will follow a brief introduction about HIV virus's biological mechanisms, and psychosocial aspects linked to HIV, which will be discussed starting from the initial phase of diagnosis through the daily self-care. In the last part, the psychosocial factors associated with the HIV-related stigma will be treated, to conclude the chapter with the issues of antiretroviral therapy and its physio-psycho-social correlates.

2.1 Epidemiology of the infection

It has been estimated that around the world 34.2 million of individuals have been diagnosed with HIV, of which 30.7 million of them are adults whereas 3.4 million are children under 15 year. In 2011, the new diagnosis have been nearly 2.5 million and the deaths for AIDS have been 1.7 million, of which 230000 were children (World Health Organization, 2012c). The data WHO (World Health Organization), UNAIDS (Joint United Nations Programme on HIV/AIDS; http://www.unaids.org/) and CDC (Centers for Disease Control and Prevention; http://www.cdc.gov/hiv/topics/surveillance/index.htm) yearly broadcast let us understand that HIV is still a plague that needs to be healed. It is not casual the use of

the word “plague,” since in the early 80’s HIV/AIDS was thought to be “a gay plague” or also called Gay Related Immune Deficiency “GRID” (Shilts, 1987). This might reflect a bias generated by the medical reports about the very first cases of HIV in fact, in such papers the authors discussed about an unknown infection (HIV) occurred in the gay men community of California. One of this reports was authored by Fannin et al. (1982; see also Masur et al., 1981), who observed, indeed, the co-occurrence of Kaposi's Sarcoma (a form of cancer) and Pneumocystis carinii Pneumonia (bacterial infection) in sexually active gay men; both diseases were hypothesized to the consequences of an unknown sexually transmitted pathogen agent. After few years, Montagnier et al. (1984), and Broder and Gallo (1984) had identified a retrovirus that the authors supposed to have caused the cases of AIDS in the gay men community, and in men and women who underwent to blood transfusions (e.g., Curran et al., 1984). Few years later, the scientific community agreed in affirming that HIV/AIDS was not just a gay related illness but also heterosexuals were at risk (e.g., Bakeman, Lumb, & Smith, 1986; Goedert, Eyster, Biggar, & Blattner, 1987). Yet, as claimed by Anderson (1992), the stigma associated with HIV/AIDS was “tightly glued” to gay men who were actually blamed for the spreading of such a new plague. After 3 decades, HIV is well-known not to be a gay-related issue nor as a stigmatized (blamed and shamed) illness, however there might be still an implicit association with gay individuals (e.g., Decety, Echols, & Correll, 2010; Naughton & Vanable, 2012). The evidence collected clearly established that there are behaviors at risk (e.g., unprotected vaginal or anal intercourse) that individuals may engage in, and this makes them at risk, not their identity (e.g., sexual identity); however, HIV stigma may be long lasting and hard-to-erase, since it is based on the stereotype that pictures gay men to be promiscuous and more prone to engage in risky sexual behaviors.

The epidemiological data about HIV diagnosis in USA, provided by the CDC (*Centers for Disease Control* and Prevention) suggests that the majority of HIV positive individuals are black, followed by white and then Latin individuals. Among men, nearly 80% of the transmissions occurred through homosexual intercourse, whereas in women, the majority (more than 80%) occurred for heterosexual contacts, and most of the individuals interviewed, contracted HIV when they were 25-33 years (CDC, 2010). The rates of HIV infections and the AIDS related deaths have been reported on table 1.

Table 1 Estimates of HIV-positive individuals, and deaths due to AIDS (CDC, 2010)

	2010	
	HIV-positive Individuals	**AIDS-related deaths**
Africa	22900000	1200000
South-East Asia	3500000	230000
Americas	3000000	96000
Europe	2300000	99000
Western Pacific	1300000	80000
Eastern Mediterranean	560000	38000
Global	34000000	1800000

Africa emerged as the country with higher rates of diagnosis and deaths; notably, the number of deaths drastically decreases from Africa to south-east Asia, to Americas, and this may also reflect the difference in the medications availability in such countries. In table 2, we have reported the data relative to specific European regions (WHO, 2010).

Table 2 Characteristics of newly diagnosed cases of HIV infection reported in the WHO European regions and by geographical area (2010)

	WHO European Region	West	Centre	East
Number of HIV cases	118335	25659	2478	90198
Rate per 100 000 population	13.7	6.6	1.3	31.7
Percentage of cases				
Age 15-24 years	12%	10%	17%	13%
Female	38%	27%	19%	42%
Transmission mode				
Heterosexual	43%	24%	24%	48%
Men who Have sex with Men	20%	39%	29%	0.7%
Injection drug use	23%	4%	4%	43%
Unknown	13%	16%	41%	6%

Note: Men who Have sex with Men is often used to indicate same-sex intercourses

In Europe, in the 2010, the majority of the new diagnoses were caused by heterosexual contacts, whereas less than a half (respectively 43% for heterosexual, and 20% for homosexual contacts) was caused by same-sex sexual contacts. Although the new diagnosis significantly increased among heterosexuals, the interpretation of the data may be misleadingly (see table 2); in fact, within the scientific report clearly emerges that the rates of HIV diagnosis increased by 18% between 2004 and 2010, and the infections caused by heterosexual contact increased by 25%, whereas among homosexual men, the rates increased by 42%. Thereby, while the majority of the new infections, in Europe, are caused by heterosexual contacts, the trend of newly diagnosed infected, sensibly increased in the general population and drastically increased among those individuals who engaged in same-sex sexual contact. Furthermore, while the overall rates of AIDS sensibly decreased in all Europe, east Europe showed increased rates of AIDS diagnosis, namely a very advanced stage of

the infection. Taken together, then, we can say claim that the individuals who engage in unprotected sex (anal, vaginal, or oral) with partners of unknown or positive HIV-status must be considered as "at risk." Nonetheless, from the reports discussed, it has emerged that individuals who actively engage in same-sex activity are still at greater risk to contract HIV. However, further clarifications are needed in order to understand this trends, namely we must focus on *behaviors* that are at greater risk, furthermore a brief description of the HIV-1 virus's characteristics is necessary. In fact, there are two strains of virus, namely HIV-1 that is quite common worldwide, and HIV-2 that is very rare except for West Africa (cf. Barroso et al., 2011). Both are transmitted through biological fluids such as blood, sperm, and more generally the biological secretions with a higher concentration of virus. Albeit the virus may be traced in the saliva, though, there is no documented infections through the contact with saliva (Cohen, Shugars, & Fiscus, 2000), nor through the pre-spermatic liquid, for which it is supposed not to be infectious for the lower concentration of virus. In effect, it has been claimed a biological plausibility of infectiousness for pre-spermatic liquid but never registered any infection through it. All the behaviors that involve contacts of mucosal tissues (e.g., oral, anal, or vaginal) with biological fluids with higher concentration of virus should be considered at risk for HIV. Accordingly, Boily et al. (2009) summarized the risk associated with heterosexual sexual contact as follows: in high-income countries, the risk to women having sex with HIV-positive men is 0.08% (0.30% in low-income countries), whereas the risk to men having sex with HIV-positive women is 0.04% (0.38% in low-income countries). Jin et al. (2010), instead, have summarized the risk associated with anal sex in gay men as follows: for insertive[4] partners, if circumcised, is 0.11% and 0.62% if not circumcised;

[4] Insertive and receptive refer to "sexual role," receptive is the partner that receives the partner's penis

whereas, for the receptive partners the risk is 0.65% if there is no ejaculation and 1.43% if there is ejaculation. In sum, receptive anal and vaginal sex are at greater risk for HIV, whereas oral stimulation of sexual organs is associated with lower risk, possibly for the presence of oral antibodies that neutralize HIV during oral sex (e.g., Hasselrot et al., 2009). Nevertheless, Sullivan, Salazar, Buchbinder, & Sanchez, 2009) claimed that 2% of the new infections in USA have been caused by oral sex and then, the risk associated with oral sex should be further debated and investigated, as it has been not fully understood. The risk of transmission from a mother to her child (called "vertical transmission") is currently drastically reduced thanks to the use of antiretroviral therapy (Namukwaya et al., 2011). After this overall epidemiological picture, it worth to say to mention that certain individuals engage in unprotected sex with casual partners, even if they are fully aware of the risk associated; the phenomenon of *barebacking*, in fact, has been largely investigated but still not fully understood.

2.2 The phenomenon of barebacking: "Who is afraid of HIV anymore?"

Individuals who engage in unprotected sex with casual partners of unknown or positive HIV status are exposed to a consistent risk of HIV and STDs; psychosocial and epidemiological data showed certain individuals engage in such risky behaviors intentionally. As claimed by Lauby et al. (2008), in USA bisexual black men who have never tested for HIV were very likely to report recent unprotected sex with partner of unknown or *perceived* negative HIV-status. Those who have never tested for HIV or who have not been tested recently, may be a source of HIV transmission to their

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and insertive is the partner that insert his penis either in the partner's mouth (fellatio) or anus (anal intercourse).

partners; despite that most of the individuals may base the decision not to use condom on the partners' serostatus perception (e.g., they think that their sexual partner could be not HIV-positive), furthermore, there is also evidence that unprotected sex can be associated with unconcern about one's and sex partners' HIV status. Both "phenomena" are very far from being rare, particularly in gay and bisexual men as documented by the studies about "barebacking" (Berg, 2009; Camoni et al., 2009; Folch et al., 2006; Pini et al., 2010; Wilton, Halkitis, English, & Roberson, 2005). This label was drawn from the equestrian term of "riding a horse without the saddle" and has been used metaphorically by (O'Hara, 1997) referred to the "condomless sex"; Parsons and Bimbi (2007), instead, strenuously claimed that bareback refers to an identity (the barebacker) rather than just to a behavior. Therefore, the phenomenon, might be better represented by a complex pattern of social, cognitive, and behavioral aspects; in fact, for instance, barebackers are not afraid to contract HIV (emotions) although they are fully aware of the risks (thoughts) (Berg, 2009). Foremost, barebackers are characterized with the knowledge of the HIV risk, which they seem to accept; while in the early ages of the HIV epidemic, individuals were not aware of the risk associated with unprotected sex now this cannot happens, as prevention interventions have been conducted and are still conducted. Thereby, now researchers are trying to understand why individuals inconsistently use condoms with casual partners, which seems to be recurrently associated with the seeking sex partners through the Internet (e.g., Berg, 2009; Parsons & Bimbi, 2007), and the abuse of alcohol or drugs (Colfax et al., 2001; Mansergh et al., 2006; Operario, Smith, Arnold, & Kegeles, 2011). This of course might permit to target the individuals who may benefit from tailored intervention, e.g., conducted online.

As hinted before, the estimate of the risk associated with unprotected sex may be composed by two aspects: the objective (evidence-based) and the perceived one (subjectively perceived), namely when individuals build an "idiosyncratic perception of risk." Accordingly, since oral sex is considered a low risk practice but, still, not safe, one may think that it is a "safe practice" instead; this could reflect also the medical changes occurred from the first cases of HIV as, indeed, risk perception is radically changed since then. In particular, there might have been a unjustified optimism after the development of Highly Active Antiretroviral Therapy (HAART), which slowed HIV progression radically, and this might have produced the erroneous perception of HIV as a curable illness (Ostrow et al., 2009; Reisner et al., 2009; Stockman et al., 2004). Nevertheless, there may be also individuals who are not comfortable with overtly discussing reciprocal HIV-status with sex partners, thus they rather "establish" it through arbitrary cues that are anchored to the HIV-individuals stereotype of someone as visibly sick, namely they may adopt the so-called seroguessing (Parsons et al., 2006). Besides, certain HIV-positive individuals might engage in barebacking (Elford, 2006; Elford, Bolding, Davis, Sherr, & Hart, 2007; Halkitis & Parsons, 2003) with a great risk for their casual partners and for themselves due to the likelihood of re-infection and co-infection, which threat their health (e.g., Colfax et al., 2004; Smith, Richman, & Little, 2005). Therefore, the phenomenon of barebacking is rather complex and likely multifaceted and certainly deserves further investigation.

2.3 The daily self-care after the diagnosis of HIV

The diagnosis of HIV may represent a trauma to which individuals could react in different ways, first of all, in fact, the reasons that led one to get tested may be very

diverse, and not everyone did it right after they contracted it. There are patients who regularly got tested some other, instead, may do it after a specific behavior, or, lastly, someone has received the diagnosis when HIV already turned into AIDS (late diagnosis). It is unlikely then to hypothesize a unique reaction to the diagnosis, since some patients might have expected it, e.g., for the risk they took; some others may did not expect it and have to deal with a psychological trauma. All of them have to deal with major changes one among others should "transit" from the *self* to the *self with HIV,* and face, then, intense psychological distress and social adjustments (Flowers, Davis, Larkin, Church, & Marriott, 2011; Davis, Larkin, Church, & Marriott, 2011). These adjustments are inextricably embedded in ones' environment and social relationships, and could change the system where patients used to live in. The first change is undeniably "psychological" and consists in the incorporation of the diagnosis within the self, together with the need to integrate the self-care in their daily routine. For instance, patients might have to adopt a healthy diet, and must use condom regularly; furthermore, they have to test the progression of the infection by blood tests and medical visits that are generally scheduled every 3/4 months. Such changes inevitably lead to perceive greater vulnerability, weakness, helplessness, defenselessness, risk, stigma, and marginalization with a consequent risk of psychological distress (De Santis & Barroso, 2011). Perry et al. (1990) suggest that the distress is transitory and that usually lasts in one month or even less; however, anxiety, depression and suicidal ideation may be still very common (Ciesla & Roberts, 2001; Coates, Moore, & McKusick, 1987; Capron, Gonzalez, Parent, Zvolensky, & Schmidt, 2012; Jia, Mehlum, & Qin, 2012). It should not be neglected that "how" the diagnosis is communicated may have an impact on patients' reactions and, long after, their well-being; thus, doctors might benefit from the collaboration with counselor or psychologists to prevent or limit negative reactions in the initial phase of diagnosis

(Hult, Maurer, & Moskowitz, 2009). However, the diagnosis is just a first challenging event that patients have to deal with; in fact, further challenging events might occur along the way and could reactivate the initial distress. In example, when patients have to start with ART medication, or when the time they have medical visits is approaching or again when they develop new relationships and must negotiate disclosure (Flowers et al., 2011). In all of these cases, the trauma caused by the diagnosis of HIV may be reactivated (e.g., Kelly, 1998; Kelly et al., 1998), since each event could remind the HIV status or recall unpleasant memories.

2.4 The physiological changes associated with HIV infection

The first changes are usually unobserved and unidentifiable and are physiological, since HIV/AIDS is caused by HIV-1 retrovirus that enters the host cells to replicate through the reverse transcriptase enzyme, which converts HIV-1's RNA in DNA. This, in its turn, enters into the cell's nucleus and incorporates to the DNA of the host cell (Paul, 2008). HIV-1 infection starts when biological fluids enter in contact with a mucosal tissue, such as anal, oral vaginal, and then HIV-1 virus starts replicating in subsets of T lymphocytes, the monocyte-macrophages, and dendritic cells that express CD4[5] and CCR5[6] on their surface (Paul, 2008). In particular, T lymphocytes that express the CD4 on their surface (CD4+ T cells) are particularly vulnerable to HIV-1 infection (O'Connell, Rabi, Siliciano, & Blankson, 2011) especially when they have been previously activated (e.g., Cole et al., 2001). Initially, HIV-1 is traceable and replicates only in the lymphoids organs (e.g., spleen, thymus, and bone marrow), which are dedicated to the circulation and production of lymphocytes (Pantaleo et al.,

[5] CD4 is a glycoprotein expressed by T lymphocytes, called CD4+, to which HIV-1 binds.

[6] CCR5 is a chemokine receptor on the white cells' surface, to which HIV-1 binds.

1993), and express sympathetic innervation and adrenoceptors; furthermore, monocytes and T cells also exhibit noradrenergic receptors (Carr et al., 1986), and the hormonal changes associated with stress (e.g., greater norepinephrine and dopamine) may activate CD4+ cells and consequently virus replication (Bellinger, Lorton, Lubahn, & Felten, 2001; Sloan, Tarara, Capitanio, & Cole, 2006; see also Cole, 2008 for a review of this mechanism). Besides, T-lymphocytes activation stimulates the production of cytokines (Torres et al., 2005) and as demonstrated by Haskó et al. (1998) catecholamine can inhibit MIP-1α (Macrophage Inflammatory Protein 1 Alpha), one of the major HIV-suppressive factors produced by CD8+ cells. This suppression is thought to occur through a β-AdrenoReceptor (β-AR) mediated mechanism. This connection may explain the association between stress and immunosuppression together with fact that HIV-1 infection progression might be promoted by the chronic immune activation; after the acute infection, viral load decreases and CD4+ cells count remain stable (Douek, 2003; Hazenberg, Hamann, Schuitemaker, & Miedema, 2000), yet CD4+ and CD8+ T-cells are both chronically activated (e.g., Simmonds et al., 1991). This chronic activation may be reflected onto the cytokines dysregulation (greater pro-inflammatory cytokines) and greater cortisol (e.g., Chittiprol et al., 2009; Lo, Mulligan, Tai, Algren, & Schambelan, 1998), which contributes to worsen individuals' health status (see Li, Yim, & Lau, 2010). Taken together, there could be more than just one physiological pathway through which HIV-1 infection worsens the immune system functioning.

2.5 Psychosocial aspects of HIV: Stigma, loneliness, disclosure, and the perception of the "future"

Together with the biological changes, the diagnosis of HIV produces psychosocial changes that may be invalidating as much as the physiological changes, and are greatly worsen by the stigma associated to HIV/AIDS. Stigma literally means "sign" and the stigmatized individuals are "signed" since they *have* or *are perceived* to have characteristics that are not socially acceptable, therefore they are "marked" (cf. Taylor, 2008). The diseases greatly stigmatized, are generally characterized with the features of progressivity and incurability, moreover they are not well understood by the general population, and symptoms cannot be totally concealed, as in the case of HIV/AIDS (Herek, 1999; Yang, 2007; Yang et al., 2007). HIV-positive individuals are also quite often blamed, because HIV is thought to be the consequence of unhealthy behaviors and therefore, it could have been avoided; sometimes, this social stigma and blame, might be both introjected by patients, with a consequent experience of psychological distress (e.g., Logie & Gadalla, 2009). Furthermore, the influence of stigma may be seen on social relationships and then, for instance, one could decide not to reveal to be HIV-positive for the fear to be rejected (e.g., Derlega, Winstead, Greene, Serovich, & Elwood, 2002) accordingly, Alonzo and Reynolds (1995) suggested an "illness trajectory" associated with HIV. It consists in 4 phases characterized by different experiences of stigma, namely (1) "at risk," (2) "diagnosis," (3) "latent," and (4) "manifest." While in the first phase the perception of stigma is related to individuals who did not test yet, the second one, "diagnosis," refers to those who have tested and resulted positive. Here, individuals may respond to perceived or enacted stigma (Scambler & Hopkins, 1986) and may experience or expect to be discriminated. In the phase labeled "latent" (Alonzo & Reynolds, 1995), HIV-positive individuals are in good health and "seemingly healthy, but doomed" (Sontag 1991, p.

119) as the infection is asymptomatic and *concealable*; the fourth stage is that of "manifest" which signs the passage to the social and physical "death." This approach may need major revisions since almost 20 years have passed, however, it can be supposed that individuals still experience different levels of stigma depending on the phase of the infection. Link and Phelan (2001), indeed, provided a more general explanatory approach, where stigma is seen as the convergence of labeling, stereotyping, separation, and discrimination acted by "stigmatizers" who have access to social, political, and/or economic power. This approach, for instance, is more general but still applicable to the current reality of HIV-context. However, not all HIV-positive individuals are stigmatized, in fact, certain ones are regarded as "innocent victims of HIV" (e.g., hemophiliacs, and babies of contracted HIV by the mothers before the era of HAART) and are thought not to be responsible for their condition, thereby they are "blameless" (e.g., Sontag 1991). Contrariwise, those who have contracted HIV through drug use or same-sex intercourse may be object of stigma due to their "deviant" behavior.

Stigma generates fear, more precisely the fear to be rejected after the disclosure of one's HIV serostatus to, e.g., partners, family, friends, co-workers nonetheless, such a disclosure may actually promote well-being for instance by providing greater availability of social-support. Moreover, disclosure is associated with the reduction of HIV transmission (Pinkerton & Galletly, 2007), since one may start using condoms more consistently (Eisele et al., 2008; Greene, Derlega, Yep, & Petronio, 2003; Simbayi et al., 2007a; Simbayi et al., 2007b). Idealistically, one may argue that the reduction of stigma might help with stemming new infections.

Interestingly, Przybyla et al. (2012) suggest that heterosexual men and women may be more likely than gay and bisexual men are to disclose their HIV status;

furthermore, disclosure is more frequent among those who has only a primary partner respect to those with only casual or both casual and primary partners. However, greater perception of stigma might keep from disclosing one's HIV status; apparently, the perception of stigma creates a barrier and promotes the isolation and the feeling of loneliness. The reduction of stigma and loneliness, then, could exert positive effects on patients' mental health (Grov, Golub, Parsons, Brennan, & Karpiak, 2010) and physical health, since loneliness in HIV-positive individuals has been associated with unfavorable CD4 + T-cells count (Straits-Tröster et al., 1994). More in general, those who are geographically isolated (e.g., rural vs. urban) could show poorest mental ad clinical profiles probably they might be characterized with lower satisfaction with life, lower perceptions of social support from family members and friends, and a reduced access to medical and mental health care. Furthermore, they could experience loneliness, and greater community stigma, as well as greater fear or rejection and more maladaptive coping strategies (Heckman, Somlai, Kalichman, Franzoi, & Kelly, 1998). Thus, although 30 years have passed since the begins of the HIV pandemic, social stigma persists and produces isolation and discrimination, which are associated with loneliness and depression, and represent harms for clinical outcome (Nachega et al., 2012). To confirm the importance of social context, Miles, Isler, Banks, Sengupta, and Corbie-Smith (2011) underlined that the interventions aimed to improve the quality of life and health of HIV-positive individuals cannot focus exclusively on the individuals, but must also focus on the local community and society as a whole.

2.6 The clinical phases of HIV infection

HIV infection is characterized with two main phases, excluding the first stage of the diagnosis, and their boundary represents a great medical and psychological divide, which separates the asymptomatic phase from the symptomatic phase. This divide generally coincides with the initiation to the antiretroviral therapy, since immune system is significantly impaired for the greater depletion of CD4+ (namely, lower than 500) and viral load drastically increases (Gazzard, 2008). Although there is no consensus about when HAART should be started, suboptimal parameters can guide clinicians' decision as for instance drastically increased viral load and decreased CD4+ counts may indicate the need to start medication (Rhame, 2011). This particular stage changes patients' lives considerably, since they have to take ART therapy daily and this may rise the perception of "being sick" with all the consequent emotional distress initially associated with the trauma of HIV diagnosis. In both phases, asymptomatic and symptomatic, HIV-positive patients have to deal with the issue of uncertainty that entails doubts about one's future and may be a pervasive source of psychological distress. More generally, the illnesses characterized with ambiguous symptom patterns, the experience of the new diagnosis and the expectations of the illness-related events generate greater uncertainty and lead individuals to engage in dysfunctional coping (e.g., Mishel, 1990). Weitz (1989) argued that uncertainty is heightened by the unpredictable physical and mental effects of the disease and this certainly produces more negative psychological adjustments (Brashers, Neidig, Reynolds, & Haas, 1998), diminished quality of life (McCain, Gray, Walter, & Robins, 2005; McCain et al., 2003; McCain & Zeller, 1996), and change in life perspective (Katz, 1996). Accordingly, Tuck, McCain, & Elswick (2008), and McCain and Elswick (2008) have confirmed that uncertainty is associated with distress, perceived stress, and lower quality of life, and could be

associate with emotion-focused coping, perhaps for the greater anxiety generated by uncertainty. Brashers et al. (1998) and colleagues (1998, pg. 67) defined uncertainty as an "individual's inability to ascribe meaning to illness when outcomes are unpredictable and when the disease and its treatments and symptoms of care are ambiguous, highly complex and lacking information." In fact, the consequence of the perception of uncertainty may be hopelessness if associated with fear or may be hope if uncertainty is associated with “wishing” (e.g., Kylmä, Vehviläinen-Julkunen, & Lähdevirta, 2001). Therefore, the stage of the illness should be adequately weighted, as it may differently affect mental health as well as physical health.

2.7 The psychological and physiological effect of HAART

In the symptomatic phase, then, HIV infection is managed pharmacologically through antiretroviral therapy and more precisely with HAART (Highly Active AntiRetroviral Therapy), which actually consists in the combination of antiretroviral medicines that act on different HIV-1 replication cycle (e.g., Gazzard, 2008). Antiretroviral therapy significantly improves clinical profile as well as psychological well-being of patients that could experience a sense of “renewed health” and “hope for living” together with greater control over their lives (Halkitis, Shrem, Zade, & Wilton, 2005; Nieuwkerk et al., 2001). Yet, the therapy is not free from physiological and psychological side effects; in fact, ART therapy has been associated with greater level of TGF-β1 or Transforming Growth Factor Beta 1 that could reactivate Epstein barr virus, which in turn could exert an oncogenic effect (Perera et al., 2011). Furthermore, lower level of viral load is expected to be associated with a reduction in pro-inflammatory cytokines production, however, even when viral load is undetectable, TNF-α may be still increased (Cervia et al., 2010). Besides, ART

medication regimens can be also very demanding physically, emotionally and interpersonally, as one may be concerned with their toxicity (Remien et al., 2006) and long-term effectiveness uncertainty, including the potential development of medication resistance (e.g., Halkitis et al., 2005). The concerns about medications (Demmer, 2003), together with fear of disclosure, substance abuse, forgetfulness, complicate regimens (e.g., number of pills required), decreased quality of life, represent all barriers to adherence as claimed by Mills et al. (2006). The authors have also individuated the facilitators of adherence, thus aspects on which clinicians could work on, such as the sense of self-worth, or seeing positive effects of antiretrovirals, as well as accepting one's seropositivity and understanding the need for strict adherence, the use of reminder tools, and a simplified regimen. In other words, it might be argued that those who are more adherent might have adapted to their new condition of "HIV-positive individual" and might have dealt positively with the changes on their identity. This could suggest that psychotherapy or psychological counseling could focus on such aspects also to prevent the risk of depression which is known to reduce significantly adherence (e.g., Rabkin, 2008), whereas the use of antidepressants has demonstrated to improve adherence with HAART (Dalessandro et al., 2007).

3. From deathly to chronic: The physio-psycho-behavioral aspects of HIV/AIDS. Their interactions and reciprocal influences.

In this chapter, we will discuss the psychosocial factors that can be associated with a worse clinical outcome in HIV positive individuals. Based on the psychoimmunological literature discussed in chapter 1, and the physio-psycho-social features of HIV-1 infection presented in chapter 2, will be here provided an overall picture of how psychosocial factors and the HIV infection can interact determining patients' health outcomes. Specifically, taking constantly into account the axiom of circularity and complexity of human-related phenomena, it will be delineated the physiological and behavioral pathways that may mediate the associations between psychological factors and HIV progression.

3.1 Sickness behavior and depression in HIV-positive individuals

The rates of depression are rather high in HIV-positive individuals (Rabkin, 2008), and may depend on several factors, from physiological to psychosocial; therefore, it is difficult and pointless to determine their "individual" effect. Contrariwise, it might be more informative to test their reciprocal interactions.

Quite frequently, HIV-positive individuals do not encounter the diagnostic criteria for major depression but they can be still diagnosed with a subsyndromal and persistent form of depression (e.g., Rabkin, McElhiney, Rabkin, McGrath, & Ferrando, 2006). It may be associated with an invalidating sense of fatigue, which might be not a mere

symptom of depression (Ferrando & Freyberg, 2008) since it could be trigged by inflammation caused by viral load and could be associated with depression (Voss, Portillo, Holzemer, & Dodd, 2007). Their relationship could be explained by their common cause, e.g., the pro-inflammatory cytokines (Capuron et al., 2009; Felger et al., 2007; Majer et al., 2008). The Tat protein (associated with the replication of the virus), in effect, induces the expression of the IDO enzyme, which in turn increases kynurenine and reduces serotonin level (Fu, Lawson, Kelley, & Dantzer, 2011). Likewise, the glycoprotein gp120, which rises TNF-α and il-6 levels, has been hypothesized to cause behavioral and endocrine abnormalities observed in HIV-positive patients, whereas Il-1 has been thought to mediate this relationship (Barak et al., 2002). The inflammation that characterizes HIV-infection may explain the comorbidity with depression however, the effect of psychosocial aspects such as stigma perception (e.g., Rao et al., 2012), and interjection (e.g., Simbayi et al., 2007a), loneliness and social exclusion (Grov et al., 2010) should be not neglected. Perceived stigma and stress, indeed, might lead to depression and therefore, a broader investigation of the physiological and psychosocial factors associated with HIV infection, and their interaction, could be explicative and would help to address depression efficaciously, also preventing non-adherence (e.g., Rabkin, 2008). In fact, for instance, greater perception of ethnic stigma has been be associated with loneliness (Doane & Adam, 2010), and social isolation (Grant, Hamer, & Steptoe, 2009), which are both related to greater cortisol, and Il-6 (Ratner, Halim, & Amodio, 2012). These physiological parameters are very harmful (also for physical health see Cole, 2008 and Dhabhar, 2000) and can promote depression (e.g., Zunszain et al., 2011), which in turn may favorite the adoption of unhealthy behaviors such as drinking, smoking, drug use, unhealthy diet. Notably, all these dysfunctional habits are significantly associated with greater TNF-α (Churg, Dai, Tai, Xie, & Wright,

2002; Ekmekcioglu, 2012); this could be then interpreted as a negative spiral where psychosocial factors may amplify the inflammation and stress, leading to depression, and unhealthy behaviors that trigger the inflammatory response, and ultimately greater risk of viral replication (e.g., Poli et al., 1990).

Depression influences behaviors, and by reducing adherence to HAART could reinforce the negative spiral as discontinued HAART may lead to failing in suppress viral load (e.g., Gross et al., 2006; Yip et al., 2006). Consequently, greater inflammatory response may be expected and, plausibly, greater levels of depression (e.g., Dantzer et al., 2008; Zunszain et al., 2011).

Cytokine-induced depression and idiopathic depression differ for some extent and despite their overall symptoms overlap, cytokines-induced depression results strongly characterized with psychomotor symptoms such as fatigue and slowed motion (Capuron et al., 2009; Bellmann-Weiler et al., 2008). However, the psychosocial factors may still concur in developing depression and whether patients suffer from subsydromal depression, cytokine-induced or idiopathic, their health may be still significantly impaired (Lyness, 2008).

3.2 Emotions and HIV progression

Emotions are characterized with specific physiological patterns, which include catecholamine and cortisol as well as pro-inflammatory cytokines; through this pathway, emotions may be responsible of faster HIV progression (§ 2.4). In fact, the primary lymphoid organs and CD4+ T cells are very sensitive to catecholamine and cytokines and in such conditions, inactive virus may start to replicate. Non-infected cells, instead, might be more vulnerable to virus infection (see Cole, 2008 for a review

of this mechanism) and in effect, negative emotions have been associated with greater viremia (Kalichman, Difonzo, Austin, Luke, & Rompa, 2002) whereas positive emotions, which promote the parasympathetic system activation (see for instance Tugade & Fredrickson, 2004), are associated with slower HIV progression. In fact, they could represent a protective factor (Moskowitz, 2003 see also Ironson & Hayward, 2008) and could favorite functional behaviors and positive re-appraisal of one's condition (Deichert, Fekete, Boarts, Druley, & Delahanty, 2008). Although emotions can be well categorized in two macro categories namely, negative and positive, it may be useful and maybe more informative to consider sub-categories, discrete emotions, and their individual effects as for instance, the "HIV-related" emotions. HIV infection, in fact, is quite commonly associated with bereavement and grief reactions caused by the disease or the loss of beloved ones because of HIV/AIDS (Goforth, Lowery, Cutson, Kenedi, & Cohen, 2009). Such emotions can cause a more rapid loss of CD4+ T-cells over time, and similarly anger (Leserman et al., 2002), shame and guilt (Dickerson, Gruenewald, & Kemeny, 2004; Dickerson & Kemeny, 2004; Dickerson, Kemeny, Aziz, Kim, & Fahey, 2004) have been associated with a faster HIV progression. Cole, Kemeny, Fahey, Zack, and Naliboff (2003) have found that irritability and hostility are both associated with social inhibition and greater sensitivity to social rejection and ultimately with a faster progression of HIV. Furthermore, individuals high on neuroticism, which correspond to emotional instability (R.R. McCrae & Costa Jr, 1997), tend to show greater worrying, fear, guilt, sadness, anger, embarrassment, disgust, and self-reported stress (Hills & Norvell, 1991). Therefore, patients characterized with high neuroticism might be at greater risk for their health because of such a negative emotional arousal, especially because emotions may amplify (negative emotions) or reduce (positive emotions) the reaction to stress. It has been documented that HIV-positive individuals tend to report greater

negative emotions than the HIV-negative individuals do (Vance, 2006); this is particularly true if they are of older age, and/or are experiencing greater loneliness, and perceive HIV-related stigma. However, the relationship among negative emotions and HIV infection may be circular, in fact, the occurrence or fear of lypodistrophia, the atypical redistribution of bodily fat caused by certain antiretrovirals, may cause worrying and emotional distress (Reynolds, Neidig, Wu, Gifford, & Holmes, 2006). Patients could, then, discontinue HAART in order to control such bodily changes; another example refers to the occurrence of diarrhea, another possible adverse effect of HAART, and the lack of control over it that are both linked to greater shame, feeling dirty, and tainted (Siegel, Schrimshaw, Brown-Bradley, & Lekas, 2010). Besides, HIV related stigma is intimately linked to emotions such as shame (Badahdah & Foote, 2010), guilt, hopelessness, and fear of discrimination (Hasan et al., 2012), and when the stigma is introjected by patients, the emotional distress could be magnified (Wolitski, Pals, Kidder, Courtenay-Quirk, & Holtgrave, 2009). Interestingly, shame and guilt, which are quite often mentioned in studies about HIV infection, are strictly related to the self and the HIV stigma, and they have been experimentally proven to impair the functioning of the immune system (Dickerson et al., 2004). This is of great interest if seen in the light of another aspect previously discussed, namely the fact that the diagnosis of HIV infection requires a transition from the self to the "self with HIV" (cf. Flowers et al., 2011; § 2.3). Thus one may hypothesize that individuals who fail in such a transition or re-appraisal of the self might be characterized with greater shame and guilt.

Perceived stigma affects emotions balance, probably through dysfunctional coping strategies such as avoidant coping (Sanjuán, Molero, Fuster, & Nouvilas, 2012), anger manifestations, lower emotional support, and greater risk of drugs use (Semple,

Strathdee, Zians, & Patterson, 2012). This can be a possible link between perceived stigma and poorer health outcomes; nevertheless, the diagnosis of HIV itself massively affects patients' emotions (Broadbent et al., 2006) and causes concerns or emotional distress and, consequently, greater negative emotions (Moss-Morris et al., 2002). Such a trauma, could explain why HIV-positive individuals tend to report greater negative emotions (Vance, 2006), together with the evidence of a neurological influence of HIV-1 virus on the process of emotions (Lane, Moore, Batchelor, Brew, & Cysique, 2012; Schulte, Muller-Oehring, Sullivan, & Pfefferbaum, 2012). Therefore, HIV-positive patients may be prone to experience negative emotions due to the stigma, loneliness, the trauma associated with the diagnosis, its daily management, and their illness representation, as well as for the neurological effect of HIV-1. The behavioral pathway accompanies the physiological pathway: individuals characterized with greater negative emotions, in fact, may tend to engage in unhealthy behaviors, whereas positive emotions may promote the adoption of adaptive and healthy behaviors. In the former case (negative emotions), individuals could try to reduce negative arousal by engaging in dysfunctional coping, e.g., drinking alcohol (Buchmann et al., 2010; Cooper et al., 1995; Pardini, Lochman, & Wells, 2004) or overeating (Evers et al., 2010), being also very likely to be not-adherent to HAART (Power et al., 2003). On the other hand, positive emotions could predict the adoption of functional coping and successful adjustment to acute and chronic stress (see Folkman & Moskowitz, 2000), confirming their protective action.

3.3 Perceived stress and HIV progression

The construct of perceived stress demonstrated to be extremely relevant, especially in HIV-positive individuals because it has been associated with shortened telomeres

(Epel, 2009; Epel et al., 2004), greater cortisol (e.g., Ebrecht et al., 2004; Pruessner et al., 1999), Il-6 (Cohen et al., 1999; Kiecolt-Glaser et al., 2003), impaired immunity (e.g., Akbar & Vukmanovic-Stejic, 2007; cf. § 1.8) and unhealthy behaviors (e.g., Ng & Jeffery, 2003; Sims et al., 2008). Accordingly, those who report greater perceived stress may show faster and greater decline in CD4+ cells count (Remor, Penedo, Shen, & Schneiderman, 2007), as well as lower HAART adherence (Royal et al., 2009). Besides, it has been hypothesized that perceived stress may be particularly influential among those who show greater Il-6 (Fumaz et al., 2012) and that are depressed (Bottonari, Safren, McQuaid, Hsiao, & Roberts, 2010), perhaps because stress amplifies depression and physiological dysregulation. Notably, HIV-positive individuals may be subjected to sources of stress that add to the "common" or "general" ones (namely, the sources of stress that anyone experience). More precisely, we refer to minority stress, which is generated by unfavorable conditions caused by the belonging to minority social groups (Meyer, 1995, 2003) and the effect of stigma-manifestations or "minority stressors" (§ 1.9). In general, all the stigmatized minority groups (e.g., sexual minority and ethnic minority) may experience greater stress but among HIV-positive patients, certain individuals are at risk for a doubled stigma. In fact, while HIV-positive heterosexual persons have to deal with stigma associated with being HIV positive gay, and bisexual individuals might have to deal with two "minorities" one associated with their sexual orientation (sexual minority) and one associated with the diagnosis of HIV. Yet, it has to be established whether this condition leads to a more compromised health. In line with Schwarz and Meyer (2010), the manifestations of stigma can influence individual well-being directly and indirectly through perceived stress; for instance, HIV-related stigma increases the perception of stress to which should be added the effect of sexual stigma for gay and bisexual HIV-positive persons. In effect, perceived stigma may generate greater

perceived stress (Remien et al., 2006); additionally, as mentioned on the first chapter, alexithymia could magnify the reaction to stress (de Timary, Roy, Luminet, Fillee, & Mikolajczak, 2008; cf. § 1.7). Therefore, individuals who perceive social stigma, might show greater stress reaction if they are also diagnosed with alexithymia. Of the four minority stressors individuated by Meyer (1995, 2003), namely enacted stigma, expectations of discrimination, concealment of one's condition or sexual orientation, and internalized stigma (e.g., Meyer, 1995, 2003; § 1.9), alexithymia might interact with the expectations of discrimination (cf. de Timary et al., 2008; Franz et al., 1999), and the increasing of stress reactions (Martin & Pihl, 1985). Thus, together with the evidence of the greater rates of alexithymia observed among HIV positive individuals possibly for the effect of HIV on the brain (Bogdanova, Díaz-Santos, & Cronin-Golomb, 2010; Fukunishi, Hirabayashi, Matsumoto, Yamanaka, & Fukutake, 1999), the risk of overreaction to stressors might be drastically increased. Furthermore, in accord with Temoshok et al. (2008), alexithymia may be associated with lower MIP-1 alpha, which is a chemokines produced by CD8+ T cells that could inhibit infection of T-cells, supported by the evidence that the administration of dexamethasone (a synthetic glucocorticoid similar to cortisol) resulted in lowered MIP-1 alpha in infants (e.g., Nupponen, Repo, Kari, Pohjavuori, & Andersson, 2002). Thereby, this provides further evidence about the role of alexithymia in increasing stress reaction and cortisol production (cf. de Timary et al., 2008).

Illness perceptions could contribute as well in increasing stress, Trovato et al. (2006; Trovato et al., 2012), in fact, found illness perceptions, and the emotional representation in particular, to correlate with greater perceived stress in patients with atrial fibrillation. Moreover, as claimed by Dohrenwend (2010), the events that are

more influential in generating stress are characterized with unpredictability and uncontrollability, and the latter refers to the beliefs about personal control and to the extent to which people believe they are in control of their destiny and important outcomes (Park & Folkman, 1997; see also Rothbaum, Weisz, & Snyder, 1982). Therefore, illness perceptions linked to the personal control actable on one's condition might buffer the effect of stressful events; this concepts can be connected with other individual aspects such as the positive attitudes towards themselves and the optimistic orientation toward the future (cf. positive thinking § 1.11). In fact, these constructs correlate with greater perception of control over events and the beliefs to possess the necessary resources to cope with stressful events (Tedeschi & Norman, 1985). Hence, positive thinking could exert a buffering effect on stress as much as social support, which might act physiologically by the activated production of oxytocin[7] (Heinrichs, Baumgartner, Kirschbaum, & Ehlert, 2003) and more generally, for the reduced reaction to stress (Olstad, Sexton, & Søgaard, 2001; Eisenberger et al., 2007). Besides, social support is associated with lower loneliness (Kwag, Martin, Russell, Franke, & Kohut, 2011), which is actually an extremely important issue in HIV-positive patients' lives and perceived social support, in fact, has been correlated with lower physical and depressive symptoms in HIV-positive persons (Bekele et al., 2012) as well as with greater hope and well-being (Yadav, 2010). The beneficial effect of social support can be also observed on stigma perception (Galvan, Davis, Banks, & Bing, 2008), therefore, it could concur in determining a more favorable mental and physical health outcome through several pathways (McDowell & Serovich, 2007). In fact, the trauma of HIV/AIDS in children is attenuated by perceived social support (Cluver, Fincham, & Seedat, 2009), although the disclosure of HIV-status itself may be stressful for the fear of associated

[7] Oxytocin is a hormone produced by the hypothalamus and released from the posterior pituitary.

rejection (Kalichman, DiMarco, Austin, Luke, & DiFonzo, 2003). Therefore, there are several aspects to be addressed with respect to social support and the underlying mechanisms.

Together with a massively activated physiological dysregulation, perceived stress can exert its negative effect through behaviors as well as dysfunctional coping as suggested by Koopman et al. (2000). Vosvick, Martin, Smith, and Jenkins (2010), in fact, have found that HIV-positive men who engaged in dysfunctional coping were more likely to develop depression over time, whereas women who engaged in self-blaming were at greater risk of depression. Interestingly, Orban et al. (2010) have examined the relation between coping and HIV progression, and have found that more unfavorable health profiles were predicted by passive coping; conversely, Martinez et al. (2012) suggested that proactive coping and spiritual coping both favorably mediate the relationship between stigma and adherence. In conclusion, Bottonari et al. (2010) observed a toxic effect of perceived stress visible only in depressed individuals, and coping strategies might not affect health outcome and adherence. However, the literature discussed seems to suggest that most of the psychosocial factors associated with HIV progression and mental health of patients could act by increasing stress.

3.4 Personality and adherence

Personality traits have demonstrated to predict health related behaviors such as adherence to HAART, in fact, Ironson, O'Cleirigh, Schneiderman, Weiss, & Costa (2008) found that the Big Five personality traits were associated with CD4+ and viremia over 4 years. The authors also found that openness and extraversion were particularly important in predicting more favorable CD4+ and viremia, whereas

conscientiousness resulted associated only with lower viremia. However, the relationship between personality traits and adherence is more complex and should be not reduced to linear association of each individual trait as the individuation of profiles may be more informative (e.g., Axelsson, Brink, Lundgren, & Lötvall, 2011). Following this approach, Ironson and colleagues (2008) have individuated profiles of patients which are associated with higher adherence namely, the "creative interactors" (high in extraversion and openness), "upbeat optimists" (low in neuroticism and high in extraversion), "welcomers" (high in extraversion and in agreeableness), "go getters" (high on conscientiousness and extraversion), and "directed" (low on neuroticism and high on conscientiousness). In opposite, the authors found the profile called "homebody" (low extraversion and low openness) that was associated with faster disease progression. However, several associations between each individual trait with HIV progression biomarkers have been individuated: neuroticism increases stress perception (Ebstrup, Eplov, Pisinger, & Jørgensen, 2011), and interacts with daily stress and may increase negative emotions (Mroczek & Almeida, 2008). Moreover, it correlates with lower quality of life, especially with its psychological aspects (Burgess et al., 2000) and has been found to correlate with lower perceived coping ability as well as with specific discrete emotions such as anxiety, fear, guilt, self-disgust, and shame, which are associated also with HIV stigma (Badahdah & Foote, 2010; Hasan et al., 2012). Conscientiousness, extraversion and openness, in opposite, have been found associated with greater perceived ability to cope with stressors, and lower perceived stress as well as positive emotions and particularly, conscientiousness showed a correlation with compassion, happiness, hope, and pride, whereas extraversion with happiness and pride, and agreeableness with happiness. Openness, instead, was associated with lower shame and fear (see Penley & Tomaka, 2002), and has been

identified as a protective factor against stress (Williams, Rau, Cribbet, & Gunn, 2009). Thus, for their connection with emotional patterns, personality traits might be linked to well-being physiologically also through catecholamine, cortisol, and pro-inflammatory cytokines. Bartley and Roesch (2011) suggested that conscientiousness exerts a protective effect against stress perception, probably by promoting functional coping strategies, especially for the adoption of problem-focused coping that, in its turn, was associated with higher positive emotions. Moreover, personality traits have been associated with the risk of depression also genetically, and as Kendler and Myers (2010) claimed a large proportion of the genetic risk for depression expressed through personality is captured by neuroticism (see also Bunevicius, Katkute, & Bunevicius, 2008). Lastly, high level of neuroticism and low level of conscientiousness have been associated with greater Il-6 production (Sutin et al., 2010); this physiological pattern may contribute to explain the association of neuroticism and conscientiousness with depression and therefore, could provide support to the relationship between personality traits and mental and physical health through perceived stress, emotions, depression, and coping strategies.

3.5 Adherence perceived self-efficacy

Thanks to antiretroviral and HAART the progression of HIV-1 infection has been drastically slowed (Siegel & Lekas, 2002) and the infection is chronically treated, which means that requires a life-long care. The extent to which patients adhere to clinical plans (e.g., scheduled medical appointments, treatment, and healthy habits) largely determines the trend of the progression over time and the patients are on the front-line of a “never-ending battle” since HIV/AIDS, to date, is still not curable. Patients should then perceive to be capable to enact the required HIV-care related

behaviors, since there are situations in which they might feel uncomfortable such as when they have to take their medication, e.g., in front of friends or in contexts in which patients do not want to reveal their serostatus. Furthermore, the degree to which illness management interferes with one's life may reduce adherence (e.g. Johnson et al., 2007); therefore, the beliefs about possessing all the necessaries capacities to be adherent are particularly important. In fact, the self-management of HIV infection comprises a wide range of behaviors and includes the taking prescribed medicine as well as the adoption of functional behaviors such as a healthy diet (§ 1.12 and § 2.3). However, the changes in individuals' daily lives associated with the diagnosis of HIV require a great amount of energy that might reduce individuals' adherence and motivation (Meichenbaum & Turk, 1987). Perceived self-efficacy, in fact, plays a crucial role in determining an efficacious self-management (Bandura, 1989; Johnson et al., 2007) and more precisely the task-specific self-efficacy is extremely relevant (Rapley & Fruin, 2001). Johnson et al. (2007) have identified two dimensions, namely integration (the treatment's integration into patients' daily lives) and perseverance (adherence to treatment regimens even when facing adversity) which are fundamental for an effective daily HIV self-management and the protective effect could be observed on depression (Bandura, 1989), which is known to reduce adherence among HIV-positive individuals (Bhatia et al., 2011). Adherence self-efficacy has been linked to lower perceived stress, and more functional coping strategies as well as lower perception of illness intrusiveness that reflect the interference with one's life (Johnson et al., 2007). Furthermore, the perceived utility of the treatment together with self-efficacy predict greater adherence (Barclay et al., 2007); thus, the beliefs about the therapy are also significant. Corless et al. (2012) investigated the effect of the general self-efficacy on symptoms perception, and found that greater self-efficacy was associated with less intense symptoms; on the contrary,

individuals who experience symptoms even when they were currently under HAART, might doubt about treatment's efficacy and could discontinue adherence (e.g., Cooper, Gellaitry, Hankins, Fisher, & Horne, 2009). Such beliefs about medication can be also associated with personality traits since physical symptoms complaint tend to be more frequent among patients high on neuroticism, and that are depressed (Howren, Suls, & Martin, 2009). Therefore, it may be predictable that patients high in neuroticism would report greater depression and maybe are more complaint about symptoms, as well as about medication and the side effects; all these aspects may ultimately increase the risk of lower adherence.

3.6 Perceived control

From the evidence discussed so far it emerges that a common protective factor is the degree of control that on perceive to exert on over external/internal events (e.g., HIV infection), and behaviors (e.g., compliance). As affirmed by Skinner (1995), the "sense of control" predicts the kind of coping one's will adopt, as well as success / failure in a wide range of life domains. The author referred also to perceived self-efficacy, learned helplessness, locus of control, and attribution theory and, as Broadbent et al. (2006) observed, personal control is highly correlated with self-efficacy in diabetic patients, and asthmatic patients. Greater controllability of illness has been, indeed, associated with greater general self-efficacy as well as with specific self-efficacy in insulin dependent diabetes mellitus patients (Griva et al., 2000). Furthermore, Moss-Morris et al. (2002) found that personal control was correlated with higher positive emotions, in line with the evidence that perceived personal control over HIV-related aspects (e.g., self-care) could predict lower risk of depression (Griffin & Rabkin, 1998; Thompson, Nanni, & Levine, 1994) and better

quality of life in HIV-positive individuals (Préau et al., 2005). Personal control, in fact, can be defined as the beliefs about the degree that the illness can be controlled (Leventhal & Crouch, 1997) and has been found by Reynolds et al. (2009) to predict the frequency and the perceived effectiveness of self-care activities and quality-of-life outcomes. Hence, individuals who perceive to be able to exert control over one's condition, and behaviors (e.g., perceived self-efficacy) may tend to be more successfully adherent with medical prescriptions (Chen et al., 2011; Griva et al., 2000; Senior et al., 2004; Petrie et al., 2011). Taken together, perceived personal control could increases well-being and reduce the risk of depression, and may lead to favorable mental and physical outcomes.

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4. Empirical contributes

In this chapter, we will illustrate the results of a series of studies we have conducted relatively to the psychosocial factors directly or indirectly connected with HIV infection. More precisely, we will start by introducing an important issue in the context of HIV-care, the rates of depression; a comparison between HIV-positive and HIV-negative individuals with respect the rates of depression and the symptomatology exhibited will be performed. Furthermore, it will be discussed the protective effect of intimate partners on depression rates. Then we will discuss the relationship between illness perceptions and the strategies of coping, describing the perceptions of illness that might influence patients' reaction to stressful events related to their illness. Subsequently, we will investigate the construct of emotions and alexithymia, which are both extremely relevant in psychoimmunology. More precisely, positive and negative emotions will be investigated through implicit and explicit instruments, and then related to the construct of alexithymia. These constructs will be ultimately correlated with the HIV-progression biomarkers. Furthermore, a work on personality types and their psychological correlates (e.g., emotions and coping strategies) will be presented. Then will be introduced the concept of minority stress in gay and bisexual men, and we will illustrate a psychometric questionnaire that we have built to assess the construct; the work has been conducted to validate the instrument that has been then used in two samples of gay and bisexual HIV-positive men. Our intent was to assess whether minority stress could be associated, with greater stress, depression and a with more unfavorable HIV-progression profile, in gay and bisexual HIV-positive men. The chapter will continue with a work on the delicate aspect of the HIV management, namely the issue of adherence to antiretrovirals. In that work we have investigated longitudinally

whether the construct of HIV adherence self-efficacy might exert a protective effect on patients' mental and physical health. Lastly, the chapter will conclude with a work in which we have investigated the psychological and physiological correlates of perceived stress in HIV-positive individuals. We have evaluated whether there were a connection between immune system activation and depression, and how perceived stress could influence physical health of patients. Within the same work, we have illustrated the psychological characteristics that might exert a protective effect against perceived stress and depression.

4.1 Depression risk and severity might be increased by HIV diagnosis but reduced by the presence of a romantic partner

Norcini Pala A., Steca, P., Sighinolfi, C., Menchetti, M.,

Abstract

Depression is an invalidating mental disorder that is very common among individuals who suffer from chronic medical illness such as HIV/AIDS, this exposes the patients to a greater risk for its psychosocial and physiological factors associated. Nevertheless, being in an intimate relationship may have a protective effect, and reduces the risk to develop depression. Therefore, the aims of this work were to verify whether HIV diagnosis and individuals' relationship status were associated with depression. Additionally, we also aimed to verify whether the symptoms of depression differed between HIV-positive and HIV-negative individuals. A large dataset (N= 1203; HIV-positive and HIV-negative individuals) was analyzed; participants completed the PHQ-9 that assesses depression and completed a brief socio-demographic questionnaire. Results indicated that HIV-positive individuals were at greater risk to be diagnosed with severe depression, whereas being in a romantic relationship may exert protective effect, as it was associated with lower risk of depression on the total sample. Lastly, more pronounced depressed mood and anahedonia along with greater fatigue were observed among HIV-positive depressed individuals suggesting that HIV-positive depressed individuals may experience more severe symptoms, including the physical symptoms of fatigue, respect to HIV-negative depressed individuals.

Key words: Depression; HIV infection; Cytokine Induced depression; Romantic relationship; Predictors of depression.

4.1.1 Introduction

Currently, depression affects about 121 million of people worldwide (WHO, 2012) and by the 2020 it was expected to cause greater disability (Davidson & Meltzer-Brody, 1999) for the severe impairment of life-quality (e.g. social, and work) and because it may ultimately lead to suicide (Rihmer & Gonda, 2012). Thereby, depression remains an important issue for primary care practitioners, especially those who clinically follow patients with chronic medical illness. In fact, chronic illness such as cancer and HIV/AIDS are associated with greater risk of depression (Ciesla & Roberts, 2001; Clarke & Currie, 2009; Rabkin, 2008), which, if occurs, contributes in worsening patients' already compromised health status (Katon & Ciechanowski, 2002). For instance, after almost more than 30 years since the first cases of HIV infection, HIV/AIDS is now treated as a chronic illness thanks to HAART (Highly Active Antiretoviral Therapy) that reduced mortality and improved expectancy and quality of life (The Antiretroviral Therapy Cohort Collaboration, 2008). However, in the context of HIV care, clinicians have to deal with patients' physical and mental illness also because depression reduces adherence with HAART, and then mental illness may influence clinical outcome through a behavioral pathway (see for instance Nyblade, 2006; Sayles, Wong, Kinsler, Martins, & Cunningham, 2009). Furthermore, depression may be promoted by infection through the activation of the dysregulation of pro-inflammatory cytokines network that concurs in reducing serotonin level (Dantzer, O'Connor, Freund, Johnson, & Kelley, 2008; Zunszain, Anacker, Cattaneo, Carvalho, & Pariante, 2011). Hence, as HIV infection produces cytokines dysregulation promoting greater levels of pro-inflammatory cytokines, it may be hypothesized that the virus itself physiologically increases the risk of depression (Dantzer et al., 2008). Cytokines-induced depression may differ from the idiopathic form of depression respect to the symptoms showed (Bellmann-Weiler,

Schroecksnadel, Holzer et al., 2008; Capuron, Fornwalt, Knight, Harvey, Ninan, & Miller, 2009), in fact, cytokine induced depression may promote more pronounced physical symptom. This work, then, has been conducted to investigate depression in individuals HIV-positive and negative.

4.1.2 The protective effect of romantic relationships on mental health

Romantic relationships demonstrated to have a "general" protective effect on individuals' well-being and are described as invaluable and irreplaceable source of strength, support, and love (e.g., Bebbington & Tansella, 1989; Gordon, Heimberg, Montesi, & Fauber, 2012; Simon & Barrett, 2010). Uecker (2012) referring to marriage, found greater level of life satisfaction among individuals who first married at younger age of 22/26 years. In general, romantic relationships profoundly influence well-being, and oppositely the inability to maintain intimate relationships is associated with emotional distress, and this may be physiologically mediated by oxytocin as claimed by Schneiderman and colleagues (2012). The authors found greater level of oxytocin in those individuals who were in a romantic relationship rather than in single individuals; according to Heinrichs et al. (2003) who found that inhalation of oxytocin reduced reactivity to stress, it may be hypothesized that romantic relationship can provide a physiological substrate for partners' well-being. In fact, reduced reactivity to stressors has been experimentally observed in individuals who were in a romantic relationship (Schneiderman, Zilberstein-Kra, Leckman, & Feldman, 2011). Cobb (1976) advocated that the effect of events that place individuals at risk for depression could be mitigated by significant others that make feel one cared for and loved and this facilitates the adoption of coping strategies and adaptation to critical situations. Loneliness impairs the self-rated physical health

(Fees, Martin, & Poon, 1999) and within the perspective of attachment theory, it has been observed that the romantic relationship enhances self-esteem and promote the adoption of healthy behaviors (e.g., Huntsinger & Luecken, 2004). Simon and Barrett (2010) have claimed the effect of intimate relationships to be beneficial for both men and women, and this effect might be not mediated by relationship satisfaction (Burns, Sayers, & Moras, 1994). That is to say, that being in a romantic stable relationship may be beneficial per se, in line with the recent finding that individuals that live alone are at greater risk for depression (Pulkki-Råback, Kivimäki, Ahola et al., 2012). Despite its beneficial effect, establishing a romantic relationship is a stressful big issue for HIV-positive individuals; in fact, even if HIV/AIDS is currently a chronic and manageable illness, some HIV-positive individuals, and their partners, may still perceive it as a deathly illness (Hoy-Ellis & Fredriksen-Goldsen, 2007; see also Greene, Frey, & Derlega, 2002; Herek & Capitanio 1999; Rintamaki & Brashers 2005). This represents a barrier and can cause reticence in engaging in romantic relationships, also for the difficulties with disclosing one's HIV-status with romantic partners that is actually accompanied by an intense fear of rejection (e.g., Relf, Bishop, Lachat et al., 2009), and loneliness that together with stigma detrimentally affect psychological well-being (Grov, Golub, Parsons, Brennan, & Karpiak, 2010). Therefore, romantic relationships may reduce the perception of loneliness and, although the quality of the romantic relationship is important as well, the "mere" perception of "not to be alone" may still exert a protective effect. Therefore, HIV-positive individuals might be at greater risk for depression also for the difficulties with building a close romantic relationship, which may add further distress and health impairment (e.g., Greene, Frey, & Derlega, 2002; Harvey & Wenzel, 2002).

4.1.3 Aims

This work was carried out to compare the prevalence of depression among HIV-positive individuals and HIV-negative individuals; HIV-positive persons were expected to show greater prevalence of depression respect to HIV-negative counterparts in line with Ciesla & Roberts (2001), Clarke & Currie (2009), and Rabkin (2008). Furthermore, HIV-positive depressed individuals were expected to show a more pronounced physical symptomatology as a result of the greater inflammation caused by the HIV infection in accord with . More precisely, the HIV-positive individuals who encounter the diagnostic criteria of depression were expected to show "sickness-behavior" symptoms. Furthermore, the protective effect of romantic relationship was tested; for the difficulties in building romantic relationships, HIV-positive individuals were expected to be less likely in a romantic relationship, additionally, we also expected to observe a significant reduction of depression risk among those who were in a romantic relationship.

4.1.4 Method

4.1.4.1 Participants and recruitment

Participants (N=1203) were HIV-positive (n = 248) and HIV-negative (n = 955) individuals; the sample was composed of men (n = 660) and women (n = 535; data missing n = 8). Of the HIV-positive individuals, the 80.41% was men and the 19.59% was women whereas, of the HIV-negative sub-sample, the 48.74% was men and 51.26% was women. The mean age was of 29.51 (DS = 6.71) years for HIV-negative sample; whereas, the mean age of HIV-positive sample was of 39.59 (DS = 8.98) years.

Participants were recruited through different sampling techniques. HIV-positive participants were recruited online through HIV/AIDS related forum, chat-room, and web-pages, as well as directly at the infectious disease department of Sant'Orsola Malpighi Hospital (Bologna, Italy). The web-based recruitment was non-probabilistic convenience sampling, and for the "offline" recruitment, we adopted a random probabilistic sampling; in fact, participants were randomly selected from the list of the daily appointments for their blood test of the infectious diseases clinic. Patients were contacted by phone and were asked whether they were interested in joining the study. In both recruitments (online/offline), participants' anonymity and confidentiality were always ensured and kept by the investigators of the study.

A modified version of snowballing technique was adopted for the recruitment of HV-negative individuals that were involved through students of the course of "emotion and motivation" of Milano-Bicocca University who received 2 extra points on their final grade. Students were instructed to recruit 50% of men and 50% women possibly not from their close relatives, nor parents, in order to reduce social desirability bias. All participants completed socio-demographic questionnaire and the PHQ-9 for the diagnosis of depression. The HIV-positive individuals recruited online completed and submitted questionnaire through Internet, whereas the HIV-positive individuals recruited offline completed and submitted a paper-pencil form of the questionnaires, and the HIV-negative individuals completed and submitted the questionnaires online.

4.1.4.2 Measures

The socio-demographic information gathered was participants' gender, sexual orientation, age, and romantic relationship status (1-engaged 2-single).

Depression was assessed through the PHQ-9 (Patient Health Questionnaire; Kroenke, Spitzer & Williams, 2001) consisting in 10 items referred to the diagnostic criteria of depression of which participants frequency from 0 (*Not at all*) to 3 (*Nearly every day*) during the prior 2 weeks (HIV-positive sample α = .85; HIV-negative sample α = 82). Diagnosis of depression was based on the categories proposed by Kroenke & Spitzer (2002) where a score from 0 to 4 indicated "no depression," from 5 to 9 indicted "mild depression," from 10 to 14 indicated "moderate depression," from 15 to 19 indicated "moderately severe depression" and score greater than 20 indicated "severe depression."

Additionally, the algorithm for the diagnosis of major depression disorder was used and consisted in DSM-VI-tr criteria of depression (APA, 2000). Thus, the diagnosis of depression was done for the participants who scored *2* on the first and/or the second item of PHQ-9, and if the total score was at least 10 (the authors stated that depression is diagnosed if 5 or more items are rated 2). The exception is the item about suicide, in fact, it should be considered even if participants rated it with 1. Therefore, the two groups individuated were, individuals diagnosed with for MDD (1) and individuals that did not encounter the diagnosis of MDD (0).

4.1.4.3 Data analysis

SPSS 15.0 (Statistical Package for the Social Sciences, Chicago, IL) was used to perform all the analyses, the chi squared was used to test the association between categorical and ordinal variables. Student t-test was used to test difference between independent groups, and it performs adequately even in case of strong departure from normality assumption (see Fagerland, 2012). Cronbach's Alpha was calculated to assess internal consistency, value greater or equal to .80 indicated good

consistency. The discriminant analysis was performed through logistic regression that, differently from discriminant analysis, is more robust to variables' departure from normal distribution and do not require the assumptions of normality (univariate and multivariate) and provides the same results as the discriminant analysis (see Pohar, Blas, & Turk, 2004). The method used was the stepwise, backward Wald.

4.1.5 Results

4.1.5.1 Sub-samples' differences on gender, age, sexual orientation, romantic relationship and depression severity

A first comparison was conducted to test difference between HIV-positive and negative samples, in fact, HIV-positive group resulted more composed by gay men (χ^2 = 240.61, p < .001) and heterosexual women (χ^2 = 7.72, p = .02). Among HIV-positive sample there were more "single" participants (not in a romantic relationship), whereas participants of HIV-negative individuals were more likely to be in a romantic relationship (χ^2 = 6.06, p = .01). HIV-positive sample resulted older than HIV-negative individuals did (t=-16.38, p < .001; M = -10.09). Based on the categories of depression severity, a comparison between HIV-positive and HIV-negative participants was performed (Table 1). Results confirmed the association between depression severity and the diagnosis of HIV (χ^2 = 34.15, p < .001), the adjusted residual (greater than |2|) indicated where the observed counts differed from the expected counts. HIV-positive individuals were more likely than HIV-negative ones, to show sever or moderately severe depression, whereas HIV-negative participants were more likely to be diagnosed with mild depression.

4.1.5.2 Characteristics of HIV positive and negative depressed individuals – Discriminant analysis

Of the participants (total sample) who provided valid responses to PHQ-9 questionnaire (n=1179), 14.77% encountered the criteria for major depression diagnosis, thus a new variable was built to discriminate depressed individuals and non-depressed individuals. The logistic regression was performed to verify the identify the variables associated with the diagnosis of depression, and the results indicated that the being diagnosed with HIV was associated with greater risk to be depressed (O-R = 2.51, $p < .001$), whereas age (O-R = .96, $p = .001$) and romantic relationships (1- single and 2-in a romantic relationship; O-R = .50, $p < .001$) were associated with lower risk. Lastly, the subsample of individuals who encountered the diagnosis of depression were selected and the logistic regression conducted helped to identify the symptoms of depression that discriminated between HIV-positive and HIV-negative depressed individuals. The results indicated that depressed mood (O-R = 1.66, $p = .03$), anhedonia (O-R = 1.57, $p = .04$), and fatigue (O-R = 1.52, $p = .05$) characterized the subsample of HIV-positive depressed participants.

4.1.6 Discussion

Depression is an invalidating mental disorder that impairs individuals' health especially if it is not correctly addressed and treated; chronic physical illness, such as HIV, increases the risk of depression (Clarke & Currie, 2009; Rabkin, 2008) in fact, it is been estimated that among HIV-positive individuals, depression prevalence is nearly almost twice respect to non-clinical population (Ciesla & Roberts, 2001). The estimation of prevalence may vary for the approaches adopted (Rabkin, 2008) as it has been observed a range of rates that goes from 5% to 50% (Berger-Greenstein et

al., 2007). However, the causes of depression in HIV-positive individuals may be several and likely, their interaction drastically increases the rates of depression; in fact, HIV infection is associated with greater physiological dysregulation, as well as social and psychological alteration, and this enhances the risk of depression (Temoshok, Garzino-Demo, Smith, & Wiley, 2011). Furthermore, the stigma associated (Grov, Golub, Parsons, Brennan, & Karpiak, 2010) with HIV may cause depression which is also associated with a more sever health impairment and among HIV-positive individuals, depression could reduce adherence to ART. This contributes in promoting HIV infection progression (Sayles, Wong, Kinsler, Martins, & Cunningham, 2009) and thus clinicians who work in HIV care contexts may have to pay particular attention to depressed patients.

In this work, depression was assessed with the PHQ-9 that allows the diagnosis of depression and to determine its severity, namely mild, moderate, moderately severe and severe and for each Kroenke and Spitzer (2002) also propose diverse interventions (e.g., follow up for those with mild depression to pharmacotherapy and the collaboration with psychiatrist of psychologist for the management of severe depression).

Our results indicate that HIV-positive individuals are at greater risk to suffer from moderate severe and severe forms of depression, which underlines the need to assess depression in HIV context. Being currently in a romantic relationship resulted associated with lower risk of depression, as well as age; the presence of intimate partner is confirmed to be a protective factors against depression, however we are aware that there may be necessary to assess further aspects related to romantic relationships (e.g. satisfaction, cohesion, and social support). So far, we may hypothesize that the simple *presence* of intimate partner may be useful and has a

positive effect on health. For instance, we suggest that clinicians may directly ask such information during the clinical interview with HIV-positive individuals and additionally we suggest PHQ-9 as an eligible and easy to use/interpret instrument in clinical settings.

The positive effect of romantic relationship may be also linked to the reduction of loneliness as well as the irreplaceable support provided (e.g., Bebbington & Tansella, 1989); for instance, intimate partners might help patients to deal with the daily management of HIV (e.g., adherence to ART). Nevertheless, it should be always considered the greater difficulties and efforts required to HIV-positive individuals in building intimate relationships also for the stigma associated with the infection and the fear of rejection (Greene, Frey, & Derlega, 2002; Herek & Capitanio 1999; Rintamaki & Brashers 2005; Hoy-Ellis & Fredriksen-Goldsen 2007; Relf, Bishop, Lachat et al., 2009). Furthermore, HIV-positive individuals may have concerns about disclosing their HIV-status and this increases the reluctance to start or seek for romantic partners (e.g., Pakenham, Dadds, & Terry, 1996). Nonetheless, no conclusions about direction of influence can be draw for our results as our study is cross-sectional; we can also confirm that there is an association between HIV-status and the likelihood of being single. The analysis conducted in the individuals who encountered the depression criteria, HIV-individuals are strongly characterized with more depressed mood, anahedonia and fatigue. This may be the result of the more severe symptomatology respect to the HIV-negative individuals and at the same time, the presence of more intense fatigue perception may be the confirmation of previous studies about cytokine-induced depression (Bellmann-Weiler, Schroecksnadel, Holzer et al., 2008; Capuron, Fornwalt, Knight, Harvey, Ninan, & Miller, 2009). In fact, this form of depression is associated with more pronounced physical symptoms.

Our study confirmed that HIV-positive individuals may be at greater risk of depression, however romantic relationship may reduce the risk to develop this mood disorder.

4.1.7 Conclusion

Depression is an important issue especially for HIV-positive individuals and clinicians who are not familiar with clinical interview or diagnosis of depression could use PHQ-9 as it is an easy and reliable instrument that allows the diagnosis of depression. HIV-care providers should do a primary screening, and in case of suspect of depression, they could refer to psychiatrists and psychologists. The need for integrating cure (antidepressants and ART) as well as psych-educative intervention emerged from our results that confirm that there are several psychological aspects that need to be addressed in the context of HIV care.

4.1.8 Limitation and future research

This work presents methodological limits that reduces generalizability of our results. Self-report measures and the recruitments adopted might contribute in confounding results. The sampling methods adopted were non-probabilistic and probabilistic; the mix of several different methods may reduce the bias of convenience sampling. For the cross-sectional nature of the study there is no way to determine any directionality respect to the associations observed, however, longitudinal study and the assessment of cytokines, cortisol and viral load may help us to understand the physiological influence of HV infection on depression.

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Table 1. Association between HIV status and depression gravity

		Depression					
					Moderately		
		None	**Mild**	**Moderate**	**Severe**	**Severe**	**Total**
HIV-negative	Count	443	335	119	41	8	946
	Adj. Res.	.0	3.4	-1.2	-3.3	-3.8	
HIV-positive	Count	109	55	36	23	10	233
	Adj. Res.	.0	-3.4	1.2	3.3	3.8	
	Total	552	390	155	64	18	1179

Adjusted standardized residual (Adj. Res.); the number of participants who provided valid responses was n = 1179

4.2 Illness perceptions and coping strategies in individuals diagnosed with HIV/AIDS

Norcini Pala A., & Steca P.

Abstract

Illness perception influence how patients react to stressful events related to their illness, which when is chronic may daily impact patients' lives. Therefore, it is worth it to explore the association between how individuals perceive their illness and how they cope with it. HIV/AIDS turned to be a chronically treated infection and despite the length and quality of life have been improved, psychological aspects related to the illness can still cause harms. This work has been conducted to explore the associations between illness representation and coping strategies, adopting a person-centered approach and considering the stage of the illness of the participants (namely, the progression of the infection). The sample was composed of 248 individuals (men and women) HIV-positive who compiled a battery of questionnaires that included Brief-IPQ that assesses illness representation and a questionnaire of 14 items that assesses coping strategies. Furthermore, HIV-related data such as viral load and CD4+ cells count was gathered. Through a cluster-analysis two groups of individuals were formed who differed on the illness perceptions features: one group was high on perceived control and low on the perceived impact of the illness on their life; contrariwise, a second group was made up by individuals characterized with lower perceived control over one's illness and greater perception of influence of the illness on their lives. These clusters were accordingly labeled as "responsive" and "succumbers." The first, characterized with greater control over one's condition, was also likely to engage in functional coping strategies (e.g., active coping), whereas succumbers, characterized with greater perceived impact on one's life, were less likely to engage in functional coping and were at risk of using alcohol to cope with adverse events linked to HIV. Moreover, succumbers also resulted to be characterized with greater viral load, whereas responsive individuals were more likely on AntiRetroviral Therapy (which reduces viral load). Our results suggest that illness representations

could be linked to the individuals' coping strategies adopted in reactions to HIV-related stressful events. Furthermore, alcohol use resulted massively used as a coping strategy, which may be extremely harmful for the patients' health.

Keywords: Illness representation; Coping strategies; Alcohol use; HIV progression; Antiretroviral medication.

4.2.1 Introduction

Chronic illnesses may be very demanding in terms of the efforts required for the daily management and for their negative effect on individuals' life, e.g., for the symptoms experienced. Currently, there are medications that turned the illness from deadly to chronic (e.g., Chu et al., 2010), however, HIV/AIDS still threaten individuals' psychosocial well-being. It should be note that the trend of the infection progression differs over time, and individually, for some extent; nonetheless, there are three main phases that can be generically identified, each of them is characterized with specific "challenges." The first phase is the "diagnosis," when patients discover to be HIV-positive and, of course, this can be extremely traumatic and may generate psychological distress, which could even turn into post-traumatic stress disorder or depression (e.g., Radcliffe et al., 2007). The "asymptomatic phase" is considered as the period in which individuals do not experience HIV-related symptoms but they still have to undergo regular screening to control infection trend. The third phase coincides with the initiation of the AntiRetroviral Therapy (ART) as the infection progressed to the point that the immune system is impaired. This phase could be the more demanding one because patients must continue with the clinical screening (e.g., every three months) and they have to take, daily, the pills prescribed (e.g., one or many, per day). Despite the limitation of this general description, which is certainly not exhaustive of the illness complexity, it substantially defines the main phases of HIV infection (see for instance WHO, 2007). Then, assuming the difference within the phases through which patients have to go through, we are interested in investigating, cross-sectionally, whether patients differ on their illness perceptions. More precisely, we aim to individuate the groups of HIV-positive individuals with similar perceptions of their illness; to the best of our knowledge this approach has been adopted for, e.g., oncological patients (cf. McCorry et al., 2012) but not in HIV-

positive patients. In fact, a more traditional variable-centered approach dominates the studies conducted in HIV-positive individuals that are more devoted to investigate the association of illness perceptions with a different set of correlates (e.g., Reynolds et al., 2009). We rather intend to identify individual differences on the perception of illness, verifying also whether these differences might explain the diverse use of coping strategies adopted when patients have to deal with illness-related adverse events. Thus, the person-centered approach sounded more appropriated since one of the major difference between the variable-centered and person-centered approach is that the first may miss the configuration of individuals' characteristics and their relative differences. However, we firmly believe that these two approaches should be considered complementary rather than alternative.

4.2.2 Illness perception

Individuals diagnosed with HIV/AIDS have to deal with major changes in their lives for the new health condition to which they must "adapt" to; the reactions to these changes may largely depend on their perception of the illness as claimed in the self-regulation model (Leventhal & Diefenbach, 1991; Leventhal, Nerenz, & Steele, 1984). This representation is based on cognitive illness-related factors such as the identity, the cause, the time-line, the controllability, the coherence, the emotional impact, and the consequences (see Kaptein & Broadbent, 2007; Lau et al., 1989). Thereby, patients build their own illness representation based on the "label," namely the nature of their condition and the cause(s) of the illness. Besides, they may anchor their representation on the illness time-line (acute or chronic) as well as on its severity, including also the perception of the cure available. Furthermore, personal control over one's condition may differ from patient to patient together with the

impact of the illness on ones' emotions (Broadbent, Petrie, Main, & Weinman, 2006; Leventhal et al., 1984). Then, we aim at investigating the illness representation in a sample of HIV-positive individuals accounting also for the illness-related conditions such as the biomarkers that indicate the progression of the infection. Although the core features of illness perception are distinct, they are highly correlated and can ultimately influence patients' behaviors (Griva, Myers, & Newman, 2000; Sacks, Peterson, & Kimmel, 1990; Senior, Marteau, & Weinman, 2004). Therefore, they may have a certain degree of predictability over patients' behavior, and this may be extremely helpful in targeting those patients who are at greater risk for dysfunctional reactions to stressful events, and that may benefit from psychosocial interventions (cf. Luyckx, Vanhalst, Seiffge-Krenke, & Weets, 2010).

4.2.3 Illness perceptions and coping strategies

Individuals who have to deal with major difficulties related to their chronic illness could ultimately adopt different coping strategies in order to act on the source of their problem, to manage the emotions generated by the stressor(s), or lastly to avoid their problems (e.g., Folkman & Lazarus, 1984). Although there are many different coping strategies (e.g., Carver & Connor-Smith, 2011), they can be categorized as problem-focused and emotions-focused (e.g., Monaci & Ricci Bitti, 1998). For instance, individuals could engage in strategies such as "engagement or disengagement," in order to act directly on the cause of distress (problem-focused) or, in the latter, to avoid problems (e.g., Moos & Schaefer, 1993; Roth & Cohen, 1986; Skinner et al., 2003). One may also adopt cognitive strategies such as the meaning focused coping (see Folkman, 2008; Morling & Evered, 2006; Park & Folkman, 1997; Skinner et al., 2003) that substantially consists in the cognitive "restructuration" and individuation

of positive meaning of the stressful events (Tennen & Affleck, 2002). However, as claimed by Culver, Arena, Antoni and Carver (2002), those who engage in emotion-focused strategies or avoidant behavior tend to show a maladaptive spiral across time; in fact, disengagement predicts distress to which individuals will respond with emotion-focused coping. In sum, coping strategies could be also defined as "adaptive" or functional coping and can be seen as a set of strategies that leads to more favorable outcomes in terms of well-being. "Maladaptive" or dysfunctional coping strategies are, instead, forms of coping that could ultimately worsen patients' condition. There is evidence of a significant relationship between illness perceptions and coping strategies; for instance, illness perception may mediate the association between physical symptoms and passive coping (Zyrianova, Kelly, Sheehan, McCarthy, & Dinan, 2011). Furthermore, patients who perceive to have greater control over their condition tend to experience better well-being (Broadbent, Ellis, Thomas, Gamble, & Petrie, 2009) and this is in line with the assumption that the perception of control over one's condition seems to be extremely influential (Chen, Tsai, & Chou, 2011; Petrie, Perry, Broadbent, & Weinman, 2011).

The identification of the profiles of individuals that differ on their perception of illness could have also a clinical relevance and may help to target patients "at risk" for dysfunctional coping and, consequently, to develop and conduct tailored interventions that would result much more efficacious (cf. Krebs, Prochaska, & Rossi, 2010). In fact, in line with Pakenham and Rinaldis (2001), who adopted the stress-coping model (Lazarus & Folkman, 1984) and defined the diagnosis of HIV/AIDS as substantially a perturbing event to which patients must adjust to. Thus, a positive re-appraisal of one's condition may lead to a more favorable psychological adjustment (Farber, Mirsalimi, Williams, & McDaniel, 2003) since the evaluation of illness as

threatening and uncontrollable might negatively influence adjustment to HIV/AIDS (e.g., Lazarus & Folkman, 1984). On the contrary, the appraisal of the illness as less threatening and controllable might be associated with better adjustment to HIV/AIDS (Anderson, 1995; Thompson et al., 1994). Seeking social support could be a functional coping strategy as well (e.g., Holt, Court, Vedhara, Nott, Holmes, & Snow, 1998), whereas the adoption of emotion-focused coping (Degenova, Patton, Jurich, & MacDermid, 1994) and avoidant coping would lead to more unfavorable well-being (Sanjuán, Molero, Fuster, & Nouvilas, 2012), probably for the maladaptive spiral that may be generated (see Culver et al., 2002). Interestingly, Chaudoir and colleagues (2012) suggested that the "spiritual peace" (e.g., religious coping) might have a protective effect on one's well-being and might be considered as a functional strategy. Therefore, coping strategies can ultimately determine a better adjustment to patients' condition of "ill-person," and they may be also connected with the perceptions of the illness. In fact, in line with a recent study conducted on patients suffering from coronary disease, illness perceptions are highly correlated with coping strategies and more precisely, personal control, whereas medication control were associated with lower disengagement; greater emotional illness representation was instead associated with disengagement (Hallas, Wray, Panayiota, & Banner, 2011). Based on this premise, through the person-centered approach, we are interested in testing whether the individuals who differ with respect to their illness perceptions, differ also on the coping strategies adopted to face illness-related adverse events.

4.2.4 Aim

The purpose of this work was to identify the main aspects of the illness perception in a sample of HIV-positive individuals, to relate them to the coping strategies adopted

by patients in relation to illness-related negative events, which they faced. More precisely, our intent was to identify groups of individuals with different illness perceptions and then to identify the core features that differentiate these groups. Furthermore, we were interested in identifying patterns of coping strategies adopted by HIV-positive individuals in relation to their illness perceptions organization. Lastly, we tested differences among groups in clinical characteristics, namely being currently on ART or naïve to ART, and the HIV-progression biomarkers (CD4+ cells count and viral load).

According to McCorry et al. (2012) we expected to find two clusters of individuals that differ on illness perceptions, one characterized with greater perceived control, the other characterized with greater perceived influence of the illness on one's life. Furthermore, for the limited evidence about clusters of HIV-positive individuals respect illness perceptions and the coping strategies, we based our hypotheses on the variable-centered approach studies. Thus, in line with Zyrianova et al. (2011), we expected more pronounced perception of HIV symptoms to correspond to greater maladaptive coping (e.g., passive); whereas, the perception of greater control was expected to be linked to functional coping (e.g., active coping), according to Broadbent et al. (2009; cf. Tedeschi & Norman, 1985). Moreover, based on the results obtained by Hallas et al. (2011), we also expected to observe greater emotional impact of illness to be associated with dysfunctional coping. The differences on illness perceptions and coping strategies, were expected to be associated with the different stages of the illness progression, which were here simplified as follows: ART was used as an indicator of the symptomatic phase, whereas greater viral load and lower CD4+ cells count were considered as indicators of a more advanced stage of the illness progression in the asymptomatic patients. Hence, we expected individuals who

presented a more advanced progression of the illness and the use of ART to be characterized with greater impact of the illness on their lives. Accordingly, dysfunctional coping strategies were expected to be more frequently adopted.

4.2.5 Method

4.2.5.1 Participants and recruitment

Participants (N = 248) were men (80.24%) and women (19.35%) while 1 participant (0.41%) did not provide this information; their mean age was of 39.59 (*SD* = 8.98) years. Participants' education included elementary and junior high school (4.04%), high school diploma (42.34%), university degree (21.77%), master's degree (13.31%), and Ph.D. or other specialization (10.48%; data missing 8.06%). The majority of the participants were currently taking ART therapy (72.58%) whereas naïve patients were 25.81% (1.61% did not provide valid response).

The sample was composed of two sub-samples recruited through different sampling techniques that will be introduced separately. The first sample (n = 158), was composed of participants recruited through a non-probabilistic web-based convenience sampling procedure that took place over 11 months, starting from September 2010. They were contacted through a post that has been published on several web sites and forums related to HIV/AIDS. On this message we provided information about the investigators, in order to increase survey's credibility, and the invitation to participate to the survey. Participants self-declared to be HIV positive and over 18 of age, they have read and agreed with a web-based informed consent on which we explained that the participation to the survey was voluntary and they were not asked to provide any sensitive information. Anonymity and information confidentiality were ensured and constantly stressed, none of them had to provide

any personal information since the questionnaires were compiled and submitted online through Internet.

The second sample (n = 90), was composed of HIV-positive patients recruited at the Infectious Diseases Operative Unit (S. Orsola-Malpighi Hospital, Bologna, Italy) over a period of five months, starting from May 2011. A randomized sampling procedure was adopted: we randomly selected five patients from the daily list of 20 patients that scheduled the clinical screening by using an SPSS algorithm. The recruitment terminated once we reached the desired sample size. However, of the participants contacted and that initially agreed to participate (n = 109), 19 (17.43%) dropped out since they received the battery of questionnaires but never gave them back to us.

Participants were informed that the participation was voluntary and all information provided would have been strictly confidential; they were also informed that anonymity would have been respected throughout all the phases of the study. Furthermore, participants received, read, and signed informed consent forms on the day of the blood test. They were also advised that the biomarkers about HIV progression would have been collected by consulting their clinical records. This study was approved by the S. Orsola Malpighi Ethical Committee.

4.2.6 Instruments

Illness perception was assessed with the Italian version of the Brief Illness Perception Questionnaire (Brief-IPQ; Broadbent et al., 2006; Italian version edited by Pain et al., 2006) composed of eight items related to the core features of the illness representation (Leventhal et al., 1984). The items were built to assess the "consequences" referred to patient's perception of the impact of the illness on

his/her life (*How much does your illness affect your life?*); timeline, namely the illness duration (*How long do you think your illness will continue?*); "personal control," one's perception of control exerted over the illness (*How much control do you feel you have over your illness?*). The "treatment control," that assessed individuals' perception of the utility of the medications (*How much do you think your treatment can help your illness?*); "identity," which corresponded to perceived intensity of the illness symptoms (*How much do you experience symptoms from your illness?*); "concern," which reflected participants' preoccupation about their illness (*How concerned are you about your illness?*); "emotions" that was referred to the extent to which patient's emotions have been influenced by illness (*How much does your illness affect you emotionally, e.g., Does it make you angry, scared, upset or depressed?*); "comprehensibility," corresponding to the extent to which patients think to have fully understand their illness (*How well do you feel you understand your illness?*). The eight items were rated on a 10-point Likert scale; higher scores indicated agreement with the statement of the item.

Coping strategies were assessed with 14 items that were built in Italian language, inspired by the COPE questionnaire (Carver, Scheier, & Weintraub, 1989), previously analyzed by Norcini Pala and Steca (unpublished manuscript) who found seven coping strategies in a large sample (N=955) of non-clinical general population. The dimensions were: (1) active coping was assessed through 2 items (e.g., *I've been taking action to try to make the situation better*); (2) seeking social support was assessed with 2 items (e.g., *I've been seeking for support from others*); (3) passive coping was assessed with 3 items (e.g., *I admitted I cannot deal with the situation and gave up attempting to cope with it*); (4) re-appraisal composed of 3 items (e.g.,

I've been trying to see it in a different light, to make it seem more positive). (5) Avoidance was assessed through 2 items (e.g., *I acted as if nothing had ever happened to me*); (6) alcohol use assessed with a single item (*I drink alcohol to make myself feel better*) as well as (7) religious coping assessed with a single item (*I've been trying to find comfort in my religion*). Participants rated the items referring to the illness-related events that they faced in the past specifying the frequency with which they adopted the coping strategy described on each item. The scale was Likert-type ranging from 1 (*Never*) to 4 (*Very often*). Norcini Pala and Steca (unpublished manuscript) previously factor analyzed these items individuating a structure partially supported by Miyazaki, Bodenhorn, Zalaquett and Ng (2008). The five latent dimensions identified have been here tested within a CFA excluding the two items individually used as indicators of alcohol use and religious coping. The results confirmed the adequacy of the dimensions (CFI/TLI = .94/ .91, RMSEA = .05, χ^2/df = 1.70) with all factors highly reliable (factor determinacy greater than .80). The loadings observed were respectively .76 and .80 for avoidance; for passive coping .53, .59 and .87, seeking social support .53 and 83, reappraisal .40, .59 and .36, active coping .55 and .66. Thus, these results supported the adequacy of the structure that has been previously identified.

HIV progression biomarkers were self-reported for the sample recruited online where participants reported the CD4+ and viral load values based on their most recent blood test; moreover, they self-reported whether they were currently taking ART. The same self-report approach has been previously adopted by Halkitis et al. (2003), and Kalichman, Rompa, and Cage (2000). For the sample recruited offline, the biomarkers were collected by consulting patients' clinical records.

Greater CD4+ cells count reflected adequate functioning of the immune system, whereas greater viral load indicated the progression of the infection. Individuals who were currently under ART should have showed undetectable viral load (e.g., lower than 50, however this value might vary for the different instruments used in biomedical laboratories). Participants who were currently taking ART were indicated on a new variable coded (1) *Yes* and (2*) No*.

In line with Gauchet, Tarquinio and Fischer (2007) CD4+ cells count was recoded and adapted to our range of CD4+ cells count; the authors included the category of CD4+ counts (1) < 200 which was absent in our sample. Hence, the data was recoded as follows, (1) > 200 and < 500 (n = 82), (2) > 500 and < 1000 (n = 126), (3) > 1000 (n = 24; missing = 16). Viral load ranged from 50 to 380000 copies/L and was recoded as (1) < 50 (to be considered as undetectable; n = 150), (2) ≥ 50 and < 1000 (n = 27), (3) ≥ 1000 and < 10000 (n = 38), and (4) ≥ 10000 (n = 17; missing = 16). Undetectable viral load meant that the infection was under control and the virus was currently replicating.

4.2.7 Data analysis

SPSS, 20 (*Statistical Package* for the Social Sciences, Chicago, IL) and Mplus 6.1 (Muthén & Muthén, 2010) were used for the analyses. The first one was used to test variables' distribution through skewness and kurtosis whereas the latter was used to perform a Confirmatory Factor Analysis (CFA) and to obtain factors determinacy (reliability) for the coping questionnaire; the method used was the Maximum Likelihood since all the variables included in the CFA were normally distributed. The Goodness-of-fit indexes were: Tucker-Lewis Incremental fit index (TLI; Tucker & Lewis, 1973), Comparative Fit Index (CFI; Bentler, 1990), RMSEA and the χ^2/df ratio (Crowley & Fan, 1997). The thresholds adopted were: CFI and TLI scores ≥ .95

indicated good fit, while scores ≥ .90 indicated sufficient fit. A RMSEA score ≤.05 indicated a good fit, whereas a score ≤ .08 indicated a sufficient fit of the model. A χ^2/df ratio ≤5 indicated a good fit for the model (Bollen, 1989; Crowley & Fan, 1997; Hu & Bentler, 1999; Schermelleh-Engel, Moosbrugger, & Muller, 2003).

SPSS 20 was then used to perform the two cluster analyses (two-step approach); one was conducted to form clusters that differed on illness perception, the other one was performed to obtain clusters that differed on coping strategies. The two-step algorithm of SPSS automatically determines the number of clusters to form, based on clusters' Euclidean distance, and Schwarz's Bayesian inference criterion (BIC) and has proven to be a valid and reliable approach as indicated by Bacher, Wenzig and Vogler (2004).

For the clusters formed respect to illness perception, the features of the clusters were tested through the Student's t test including in the test each item of the illness perception questionnaire. This approach was chosen since only two clusters were extracted. Whereas, for the clusters formed respect to coping strategies, we conducted a discriminant analysis in order to identify the strategies (their linear combination) that maximally discriminated between the clusters formed. This approach was adopted since the clusters formed were three. The stepwise method with the Wilk's Lambda criterion was used (see Barbaranelli, 2006) and the Box test was requested to test homogeneity of variance (H_0 = the variances are equal), eigenvalue indicated the proportion of variance explained, and Wilk's Lambda indicated the significance of the discriminant function.

Lastly, cross-tab with χ^2 was used to test the association between clusters and HIV-progression biomarkers, ART therapy, and to test the association of the illness

perception clusters with the clusters related to the coping strategies. The adjusted residual was used to individuate the significant difference respect to expected/observed counts, where values greater than |2| indicated a significant difference.

4.2.8 Results

4.2.8.1 Illness perception - Cluster analysis

In order to individuate profiles of individuals who differ with respect to their perception of HIV, we conducted a two-step cluster analysis including the eight items of the brief version of IPQ. Two clusters were automatically formed (in line with BIC change that resulted: from 1 to 2 clusters -64.17, from 2 to 3 clusters .43, from 3 to 4 clusters 10.03). As showed in table 1, individuals in cluster 1 were characterized with greater control and trust on ART, whereas individuals in cluster 2 were characterized with greater concerns about their condition, as well as perception of greater impact on their life and emotions, and greater experience of symptoms. Notably, no difference was observed respect to timeline and coherence (see Table 1). The two clusters were labeled accordingly, referring to the scores on the IPQ items on which the individuals differed; in particular, cluster 1 was named “responsive,” and the second one was labeled as “succumbed.” In fact, the first cluster was characterized with greater perceived control over one’s condition as well as greater perceived utility of medications, whereas the second cluster resulted characterized with greater influence on one’s life caused by HIV and very low perceived control, then considered as “overwhelmed by illness.”

4.2.8.2 Differences between "Responsive" and "Succumbed" in HIV-related variables

We then tested whether the two profiles were differently associated with the HIV progression biomarkers and use of ART; no significant association was found with the CD4+ cells count (χ^2= 1.83, p > .05), whereas the clusters were significantly associated with viral load (χ^2= 8.02, p = .046). The adjusted residuals confirmed that those patients with greater viral load were more likely to be labeled as "succumbed" (which actually was the only residual > |2| for the individuals with viral load greater than 10000 copies/L that we coded as *4*). Moreover, there was a significant association between the clusters and the use of ART (χ^2= 5.16, p = .023), namely those who were currently taking ART were more likely to belong to the cluster of "responsive" whereas those who were naïve to ART were more likely to belong to the cluster of "succumbed" (residuals were the same for each cell: |2.4|).

4.2.8.3 Coping strategies - Cluster analysis

The cluster analysis conducted with the coping strategies was aimed at identifying groups of individuals that differed respect to the patterns of coping strategies adopted. Three clusters were formed (in line with BIC change that was: from 2 to 3 clusters -22.22, from 3 to 4 clusters 17.90) and through the discriminant analysis, we individuated the functions that maximally discriminated between the clusters. Two functions identified (eigenvalues were 4.30 and 1.26) were both significant (Wilk's Lambda for both functions: λ=.08, p < .001, and λ=.44, p < .001; varimax rotated) and have been reported on table 2; the function 1 corresponded to the use of alcohol to feel better, and the function 2 corresponded to the functional coping strategies (see table 2).

Based on these results, we labeled clusters 1 “dysfunctional copers” to capture the lower scores on functional coping strategies (e.g., low active coping, and high passive coping). Cluster 2 was labeled as alcohol users since together with greater passive coping, alcohol use to cope with problems was extremely high on this cluster. Lastly, cluster 3 was labeled “functional copers” since individuals in this cluster resulted with higher score on seeking social support, active coping, moderately high on re-appraisal and religious coping (cf. table 3).

4.2.8.4 Coping, HIV biomarkers, and illness perception

Subsequently, we tested whether the clusters referred to coping strategies were associated with the HIV biomarkers and with the ART medications. No differences were found with respect to CD4+ cells count ($\chi^2 = 1.36$, $p > .05$) nor with viral load ($\chi^2 = 8.69$, $p > .05$), whereas individuals who were more likely to be in the cluster of alcohol users ($\chi^2 = 10.98$, $p = .004$; adjusted residual $|3.4|$). Furthermore, we tested whether individuals in the clusters related to the illness perceptions differed on the coping strategies adopted. In fact, individuals of the cluster “succumbers,” namely those who experienced greater impairment of their lives due to HIV, were very likely engage in alcohol use as a coping strategy, whereas those who were “responsive” were more likely to engage in functional coping ($\chi^2 = 12.39$, $p = .002$; see table 4).

4.2.9 Discussion

Great strides have been made to reduce the medical threat associated with HIV but more is still left to do with respect to the psychosocial aspects related to the illness. One principal aspect of chronic illness is that individuals are the principal *actors* (intended as those who act against and to promote their health) of the clinical path,

they have to follow in order to control the progression of the infection. The diagnosis of HIV produces inevitable changes in patients' life, and requires greater efforts to adapt to the "new condition" of an ill-person (cf. Pakenham & Rinaldis, 2001) and if one fails in such an adaptation, well-being might be drastically compromised. The centrality of individuals in managing their clinical condition is underlined by the aspects related to the HIV progression and more precisely alcohol use that have been previously found to be extremely dangerous for its effect on CD4+ cells count (Baum, Rafie, Lai, Sales, Page, & Campa, 2010) as well as on adherence (e.g., Chander, Lau, & Moore, 2006). Therefore, the understanding of how patients act when they face HIV-related stressors may be extremely important as t could contribute in preventing dysfunctional behaviors, which ultimately lead to unfavorable clinical outcomes. The approach we used in this work is called "person centered" and, as such, it focuses on individuals' difference contrarily to variable-centered approach; we decided to adopt the person-centered approach to verify how HIV-positive patients differ respect to their illness perceptions and if this difference corresponded to diverse coping style and stage of the illness. In fact, in this work, the person-centered approach allowed us to acquire information about different configurations of patients' illness perceptions. Furthermore, the core features referred to illness representations (see Leventhal & Diefenbach, 1991; Leventhal, Nerenz, & Steele, 1984) have demonstrated to discriminate between two profiles of patients that have been labeled "responsive" and "succumbed," two labels used to capture the peculiarity of the clusters. This result is in line with McCorry et al. (2012) who found two clusters that were very similar to those we found in current work, remarkably, despite the different populations (oncological patients vs. HIV-positive patients) the results substantially overlap. The clusters found have been labeled *responsive* to identify the individuals who perceive to be capable to face the difficulties associated with their condition also showing

lower perception of illness intrusiveness on their lives. Whereas *succumbed* ones may tend to complain about the impact of the illness on their lives, and show lower perception of control over their condition. No differences were observed about comprehension and time-line of the illness, and this may reflect the fact that patients are told from the very start (the diagnosis) that although HIV is not curable, it can be only chronically treated; hence, this aspect might be not influenced by idiosyncratic interpretation. It is interesting to note that such (reasonable) complaints came from the individuals who were not currently taking ART medication, and more precisely from those who showed greater viral load. Possibly, they might have been experiencing greater symptoms, which actually could have increased the perception of illness intrusiveness. This result is in line with Rivero-Méndez and colleagues (2009) who found greater symptoms perception and complaints in HIV positive who were untreated. Either way, it cannot be ignored that ART medication symbolically represents an obstacle, but also the only "instrument" that patients possess to fight the infection. For the cross-sectional nature of this work no directionality can be determined; however, we hypothesize a probable explanation of the results obtained. We suggest that the individuals who are on ART may perceive to "do something concretely to fight the infection" whereas those who are not treated, and experienced greater viral load, may experience their condition more "passively." In fact, patients who are not treated have "only" to undergo to medical screening regularly, generally three-monthly but not daily, whereas individuals on ART take medication daily, we suggest this to promote the perception of doing something to fight the infection. Further investigation may help to explore our hypothesis, including, for instance, specific assessment about the perception of ART.

As claimed by Pakenham and Rinaldis (2001), in a prospective of stress-coping framework, the cognitive appraisals of HIV/AIDS massively affect patients' adaptation to illness and their reactions (cf. Hallas et al., 2011). In fact, respect to the coping strategies, we individuated three groups of individuals, coherently with the person-centered approach adopted; they resulted differently characterized respect to the functional/dysfunctional (passive coping) coping, and alcohol use, the latter, alone, actually accounted for greater variance among the clusters. In line with the results, the clusters have been labeled as "functional copers," "dysfunctional copers," and "alcohol users." The latter cluster was also characterized with more passive coping and very low religious coping. Functional and dysfunctional copers, instead, mainly differed on the extent to which individuals adopted "active coping," dysfunctional copers, indeed, scored lower on most of the functional coping strategies. Further investigations are needed to understand and to establish the patterns of coping that can characterize HIV-positive individuals more exhaustively, also longitudinally. So far, based on our results, we suggest that the patients that show a more responsive attitude towards their condition and perceived to be able to exert a certain degree of control over their illness, are more likely to engage in functional coping strategies. This result is in line with the literature (e.g., Tedeschi & Norman, 1985) showed that patients who perceive to exert control over their condition also perceive to have the necessary resources to cope with stressful events. In opposite, those who were greatly affected by the illness, also complaining greater illness intrusiveness, resulted at risk to engage in dysfunctional coping and in particular to use alcohol. We suppose this to be related to the need of reducing emotional distress caused by the illness; furthermore individuals naïve to ART were at greater risk to use alcohol as a coping strategy, and this is particularly relevant since alcohol use may negatively affect physical health as may reduce CD4+ cells

count (Pol, Artru, Thepot, Berthelot, & Nalpas, 1996), and affects neurological functions (Meyerhoff, 2001). Moreover, even moderate use of alcohol before sexual intercourse predicts unprotected sex among HIV positive individuals (Kiene, Simbayi, Abrams, Cloete, Tennen, & Fisher, 2008). This may then expose both sex partners to the risk of infection, re-infection or co-infection, with major negative effect on physical health.

Overall our findings confirm, coherently with the literature, that control over one's condition is one of the most important aspect of illness perception (Chen, Tsai, & Chou, 2011; Petrie et al., 2011), which more likely determine the coping strategies adopted by patients in response to stressful events related to their illness. The typological approach used in this work offers insights on the relative weak importance of certain aspects such as the time-line and the comprehension. It seems plausible to suggest that perceived control "control" might be one of the core aspect on which clinicians could work on with HIV positive patients in order to ensure a better clinical outcome, avoiding the occurrence of dysfunctional behaviors such as alcohol use.

4.2.10 Limitations and future studies

The present work has few methodological limitations, in fact, for one of the two samples the convenience non-probabilistic was used, and this may limit the generalizability of the results. Moreover, the use of self-reports (including the data about HIV-progression) may be partially reliable; thus, it may be more desirable to use external observation or clinical records when possible. Furthermore, this study is cross-sectional; hence, we just can hypothesize the directionality of the relationships observed. We intend to evaluate the classification obtained in this work

longitudinally, and we are interested in understanding the perception of ART perception more deeply by assessing the advantage and disadvantage perceived by patients. Furthermore, it seems very important to understand how the dysfunctional coping linked to alcohol use might influence the clinical outcome as well as mental health.

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Table 1 Clusters difference on IPQ items (Student's t test, and means)

	Cluster 1	Cluster 2	T test
How much does your illness affect your life? (consequences)	3.74	**7.27**	-12.34***
How long do you think your illness will continue? (time-line)	7.97	8.42	-1.37 NS
How much control do you feel you have over your illness? (personal control)	**7.20**	5.41	5.34***
How much do you think your treatment can help your illness? (treatment)	**9.20**	8.12	4.47***
How much do you experience symptoms from your illness?(identity)	1.72	**3.53**	-7.58***
How concerned are you about your illness? (concern)	4.07	**7.79**	-13.90***
How well do you feel you understand your illness? (comprehensibility)	7.30	6.82	1.55NS
How much does your illness affect you emotionally, e.g., Does it make you angry, scared, upset, or depressed? (emotions)	3.54	**7.73**	-13.24***

*ns non-significant; *** p < .001*

Table 2 Rotated structure of the discriminant analysis, and unstandardized canonical discriminant functions

	Functions	
Coping	1	2
Alcohol use	.95*	.06
Active	-.14	.77*
Re-appraisal	-.05	.43*
Seeking social support	-.01	.32*
Religious coping	-.07	.23*
Passive	.15	-.16*
Unstandardized canonical discriminant functions		
Cluster 1 "Dysfunctional copers"	-1.09	-1.44
Cluster 2 "Alcohol users"	3.58	.30
Cluster 3 "Functional copers"	-1.26	1.13

** variable included in the function*

Table 3 Clusters Fisher's linear discriminant functions

	Clusters		
	1	**2**	**3**
Passive	1.76	1.99	1.48
Seeking social support	1.05	1.48	1.46
Re-appraisal	4.24	5.05	4.86
Active coping	5.01	6.18	7.14
Alcohol use	18.82	37.26	20.08
Religious coping	.78	.02	1.68

Table 4 association between clusters of coping and IPQ

	Clusters coping		
Clusters IPQ	**Dysfunctional copers**	**Alcohol users**	**Functional copers**
Responsive	27	8	38
Adj. Res.	.2	**-3.3**	**2.7**
Succumbers	50	44	47
Adj. Res.	-.2	**3.3**	**-2.7**

4.3 Exploratory investigation of explicit and implicit emotions' dimensionality and their relationship with alexithymia and HIV progression biomarkers

Norcini Pala A., & Steca P.

Abstract

Emotions are part of everyday life and play a role in motivating behaviors and in promoting or, oppositely, in worsening well-being. The literature about emotions raised questions about the dimensionality of this construct; based on several studies that showed emotions' peculiar physiological pattern, within the category of emotions there might be sub-categories of emotions with a strongest and specific effect on health. For instance, certain negative emotions (e.g., shame and guilty) have been associated with immune system impairment, which is also influenced by alexithymia that in its turn could promote the experience of greater negative emotions as well. With this work, we aimed at exploring emotions' dimensionality, and at investigating the relationship between implicit and explicit emotions and alexithymia. Then, the relationships of such dimensions with HIV-progression biomarkers have been ultimately tested. Two datasets of two different studies (one of which was conducted on HIV-positive individuals) were analyzed, and the results showed that explicit emotions may be better explained by a second order factorial model (positive and negative emotions) with first order factors including specific sub-categories of emotions. Additionally, implicit negative and positive emotions were associated with the six first order factors related to explicit emotions (three negative and three positive). Two of the three dimensions of alexithymia were confirmed and resulted significantly associated with negative and positive emotions, both explicit and implicit. Furthermore, in line with previous studies, only certain discrete emotions (first order factors, underlying the second order negative emotions) were associated with worst HIV progression biomarker profile.

Key words: Emotions; Implicit and explicit assessment; Alexithymia; HIV/AIDS

4.3.1 Introduction

Emotions are inextricably present in everyday life, and although most individuals are able to face them, some individuals may do not, possibly because they fail in processing emotions cognitively. From the knowledge collected so far, we know that emotions are complex elements that are the result of the interactions between subjective and objective factors, mediated by neural-hormonal systems (Kleinginna P. & Kleinginna A., 1981), and may act as motivators of behaviors (e.g., Izard, 2010). Emotions have been conceptualized as composed a finite number of discrete emotions (e.g., happiness, sadness, disgust, anger, fear, and surprise; Ekman et al., 1987) and as psychological factors operatively categorizable through the two basic dimensions of "valence," and "arousal" (Russell & Barrett, 1999). While valence varies from negative, to neutral, through positive values, arousal stands for the intensity of emotions, and varies from very low to very high (Viinikainen et al., 2010). Howsoever, such supposed "positive/negative" polarity might be too restrictive, and a complex hierarchical structure may be more adequate (e.g., Mehrabian, 1998). The assessment of emotions is generally conducted through self-report instruments that refers to explicit emotions, nevertheless, some authors claimed the need to assess emotions also implicitly (e.g., Quirin, Kazén, & Kuhl, 2009). Although implicit and explicit emotions might be correlated, they could act differently and independently on health (Gawronski, LeBel, & Peters, 2007; Hofmann, Gawronski, Gschwendner, Le, & Schmitt, 2005). For instance, Quirin et al. (2009) have argued that individuals have a general stable tendency towards positive or negative affectivity, which can be better captured implicitly rather than with explicit self-report questionnaires that could be influenced by confounding factors (see also Robinson & Clore, 2002). Quirin et al. (2009), in fact, claimed the utility of adopting stimuli that automatically

activate emotional representations (see also Fazio & Olson, 2003; Strack & Deutsch, 2004). Thereby, a brand new instrument capable to evaluate individuals' emotions indirectly through the presentation of non-sense artificial words (e.g., "SAFME") of which one must rate the "emotional" sound, namely the extent to which the words sound happy, cheerful, energetic, helpless, tense, inhibited. Through this approach the authors found that cortisol dysregulation was predicted by implicit but explicit emotions (see also Lai et al., 2005; Steptoe et al., 2007). This work, then, it is focused on the investigation of the dimensionality of explicit and implicit assessment of emotions, and their reciprocal associations.

4.3.2 Emotions and health, and their association with HIV/AIDS progression

The importance of evaluating emotions comes from the studies that have demonstrated how emotions can be related to individuals' health. Positive emotions, for instance, are associated with longevity and subjective well-being (Diener & Chan, 2011; Xu & Roberts, 2010) as well as with lower risk of coronary heart disease (Davidson, Mostofsky, & Whang, 2010) whereas negative emotions have been linked to greater risk of coronary heart disease (e.g., Smith, Glazer, Ruiz, & Gallo, 2004). For their contribution in determining the health outcomes, emotions are an important target of health psychology, especially when it comes to individuals suffering from chronic diseases. In this paper, we focused our attention to a specific chronic disease that is still an actual issue, HIV/AIDS illness that is caused by the infection of HIV-1 virus responsible of the immune system impairment (principally affecting leucocytes such as CD4+ cells). There is evidence that emotional distress is associated with greater viremia (Kalichman, Difonzo, Austin, Luke, & Rompa, 2002)

and that negative emotions such as hostility, irritability, and jittery might be associated with lower CD4+ cells count (Cole et al., 2003; Leserman et al., 2002). These associations can be interpreted in the light of the influence of emotions on individuals' behavior, and the physiological pattern correlated with emotions. Negative emotions, indeed, have been linked to dysfunctional coping such as alcohol use (Buchmann et al., 2010; Cooper et al., 1995; Pardini et al., 2004) and poorest adherence to antiretroviral medications (Power et al., 2003). Positive emotions, instead, promote healthy behaviors, also favoring the adoption of restorative activities (Bardwell, Berry, Ancoli-Israel, & Dimsdale, 1999; Fosse, Stickgold, & Hobson, 2002; Smith & Baum, 2003). At the same time, there might be a physiological pathway through which emotions could act, namely through immune activation and inflammation, which may lead to HIV-1 replication (see Dickerson, Gable, Irwin, Aziz, & Kemeny, 2009; Poli et al., 1990). Moreover, negative emotions promote greater cortisol production, a glucocorticoid that is very detrimental for its immunosuppressive effect (Buchanan, al'Absi, & Lovallo, 1999). Thus, at least two pathways through which emotions can influence HIV progression can be hypothesized; therefore, in this work, we will investigate the relationship between emotions and the HIV progression biomarkers.

4.3.3 Emotions and alexithymia

The distinction between implicit and explicit assessment of emotions is much more relevant when respondents have difficulties to process their emotions, showing difficulties with identifying and/or describing them. Those who suffer from alexithymia, in fact, are characterized with a significant impairment in the

understanding, processing, and describing emotions (Taylor, Bagby, & Parker, 1999); consequently, emotional stimuli may provoke an autonomic activation despite one is not aware of that (Lane et al., 1997; see also Köhler & Moscovitch, 1997) and might perceive a general state of "distress." This could explain why alexithymic individuals usually report greater negative emotions (Lumley, Mader, Gramzow, & Papineau, 1996; Palmer, Donaldson, & Stough, 2002).

As previously hinted, the construct of alexithymia is characterized with two main features: the lack of awareness about one's emotions and the inability to describe them (e.g., Bagby, Parker, & Taylor, 1994; Haviland, Shaw, Cummings, & MacMurray, 1988) and there is consensus in considering alexithymia a risk factor for health. In fact, for instance, it has been linked to more pronounced production of Il-6 and TNF-α (Bruni et al., 2006; Honkalampi et al., 2011; Temoshok et al., 2008), which are both extremely harmful for HIV positive patients (Poli et al., 1990). Temoshok et al. (2009), indeed, observed that alexithymia was associated with HIV progression over time, and this might be extremely harmful since alexithymia is frequently diagnosed in HIV-positive individuals, perhaps for the effect of HIV-1 virus on the brain (Bogdanova, Díaz-Santos, & Cronin-Golomb, 2010; Fukunishi, Hirabayashi, Matsumoto, Yamanaka, & Fukutake, 1999). Accordingly, we will test the association between alexithymia and HIV progression biomarkers.

4.3.4 Aims

This work aimed to investigate the dimensionality of the negative and positive emotions assessed explicitly, testing also their associations with emotions assessed implicitly; furthermore, for both, implicit and explicit emotions, it has been also tested the association with alexithymia. To explore and confirm explicit emotions'

dimensionality (e.g., negative / positive *vs.* discrete emotions) we adopted a stepwise approach (e.g., Anderson & Gerbing, 1988; Newcomb, 1990), therefore, the dimensionality of the explicit assessment of emotions was tested, and then the dimensions were correlated with implicit emotions. Besides, we also tested the association between alexithymia and implicit and explicit emotions; then, these same associations have been evaluated on a sample of HIV-positive individuals, in which we included the biomarkers of the HIV-progression as well. Based on the literature reported above, we expected to find explicit and implicit emotions to be significantly associated (Quirin et al., 2009) and both were expected to be related to the factors underlying the construct of alexithymia expecting the latter to be associated with greater negative emotions and lower positive emotions, explicit (e.g., Parker, Prkachin, & Prkachin, 2005) and implicit (e.g., Lane et al., 1997; Lumley et al., 1996; Palmer et al., 2002). Furthermore, hypothesizing that alexithymia would promote greater implicit autonomic activation (Lane et al., 1997) we expected to observe an indirect association between the factors underlying alexithymia with negative explicit emotion, mediated by negative implicit emotions. This hypothesis was inferred for the assumption that alexithymic individuals are unable to recognize and report emotions, and commonly experience a generalized arousal interpreted as "negative emotions" (cf. Lumley et al., 1996; Palmer et al., 2002). Negative and positive emotions were expected to be correlated with the HIV progression biomarkers and more precisely, negative emotions (implicit and explicit) with lower CD4+ cells count and greater viral load, whereas positive emotions were expected to correlated with greater CD4+ cells count and lower viral load (e.g., Cole et al., 2003; Dickerson et al., 2009; Kalichman et al., 2002; Leserman et al., 2002; Power et al., 2003). Moreover, in line with Temoshok et al. (2008) we expected to observe an association between the factors underlying alexithymia and more unfavorable HIV-progression

biomarkers; lastly, we verified whether HIV positive individuals scored higher on alexithymia than HIV-negative individuals, in line with Bogdanova et al., (2010), and Fukunishi et al. (1999).Two datasets have been analyzed, the first and larger one (HIV-negative individuals) has been used to test the emotions' dimensionality and the associations between the dimensions assessed (implicit and explicit emotions and alexithymia dimensions). The second dataset (HIV-positive individuals) has been analyzed to confirm the results of study 1 and to test the relationship of the dimensions assessed with the HIV progression biomarkers.

Study 1

4.3.5 Method

4.3.5.1 Participants and recruitment

The participants (N = 955) were men (48.48 %) and women (50.99%; data missing .53%) with a mean age of 29.51 years (SD = 6.71), and their education included junior high school (5.34%), high school diploma (53.50%), university degree (19.69%), master's degree (17.49%) and Ph.D. or other specialization (2.83%; data missing 1.15%).

Participants have been recruited with the snowballing sampling technique by students of the course of "emotion and motivation" of Milano-Bicocca University, who received two extra points on their final grade. Students were instructed to recruit 50% of men and 50% women, none of which should have been their closest family (e.g., relatives or parents) in order to reduce social desirability. All participants completed and submitted a battery of questionnaires through Internet and self-declared to be over 18 years old.

4.3.5.2 Instruments

Explicit Emotions were assessed with the Positive-And-Negative-Affect-Schedule (PANAS; Watson et al., 1988). Participants rated each of the 20 emotions listed using a Likert scale from 1 (very slightly or not at all) to 5 (extremely).

The *Implicit Positive And Negative Affect Test* (IPANAT; Quirin et al., 2009) was used to assess *implicit* emotions; it has proved to be a reliable method for the assessment of stable individual differences in implicit emotions as IPANAT assesses them indirectly. In fact, participants rated the extent to which six artificial words (SAFME, VIKES, TUNBA, TALEP, BELNI, and SUKOV) expressed six emotions: happy, cheerful, energetic and helpless, tense, and inhibited on a Likert scale: (1) *doesn't fit at all*, (2) *fits somewhat*, (3) *fits well*, and (4) *fits very well*. Participants rated the "sound" of each word on each of six emotions, the implicit assessment of positive and negative emotions is obtained by computing the sum of the means of the three positive emotions (implicit positive emotion) and negative emotions (implicit negative emotions). The instrument showed good reliability and resulted significantly correlated with positive and negative emotions assessed explicitly (Quirin et al., 2009). This measure is to be considered "implicit" since individuals are unaware of the construct being measured (see De Houwer, 2006; Fazio & Olson, 2003).

Alexithymia was assessed with the Toronto Alexithymia Scale (TAS-20; Bagby et al., 1994) composed of 20-item graded from one to five, referring to three dimensions: difficulty in identifying feelings (DIF), difficulty in describing feelings (DDF) and externally oriented thinking (EOT).

4.3.5.3 Data Analysis

The analyses were performed with SPSS 15.0 (SPSS Inc. Chicago, IL, 2006) and Mplus 6.1 (Muthén & Muthén, 2010); the former was used to calculate skewness and kurtosis to assess variables' distributions (if lower than |1| were treated as normally distributed, if greater than |1| were treated as non-normally distributed). Mplus 6.1 was used to perform the E-SEM (Exploratory Structural Equation Modeling) to explore the dimensionality of PANAS and the CFA (Confirmatory Factor Analyses) was performed to confirm the latent dimensions found within the E-SEM. The SEM (Structural Equation Modeling) was conducted to test the associations between the negative and positive emotions (implicit and explicit), and alexithymia. All these analyses were performed by using the Weighted Least Square Method (WLSM), since some variables violated the assumption of normality. The Goodness-of-fit indexes adopted were the Tucker-Lewis Incremental fit index (TLI; Tucker & Lewis, 1973), the Comparative Fit Index (CFI; Bentler, 1990), RMSEA and the χ^2/df ratio (Crowley & Fan, 1997). CFI and TLI scores ≥ .95 indicated good fit, while scores ≥ .90 indicated sufficient fit. A RMSEA score ≤.05 indicated a good fit, whereas a score ≤ .08 indicated a sufficient fit of the model. A χ^2/df ratio ≤5 indicated a good fit for the model (Bollen, 1989; Crowley & Fan, 1997; Hu & Bentler, 1999; Schermelleh-Engel, Moosbrugger, & Muller, 2003).

4.3.6 Results

4.3.6.1 *Explicit emotions' dimensionality (PANAS)*

The intent was to verify whether the bi-factorial model (positive and negative emotions) of PANAS was adequate, and the results obtained with the CFA disconfirmed the adequacy of the bi-factorial model (CFI/TLI .908/.897, RMSEA =

.108, χ^2/df = 11.69). Thereby, in order to explore the dimensionality of PANAS, we proceeded by performing an E-SEM and to obtain more robust results, the sample (N=955) was randomly divided into 2 sub-samples through the algorithm of SPSS 15.0. On the first sub-sample (n = 491) the E-SEM has been performed, and the dimensions obtained were then tested on the second sub-sample (n = 464) through the CFA. The E-SEM allowed to test the three dimensions related to PANAS positive emotions (joy, interest, and activation) that Egloff et al. (2003) previously found, and since no references were found about the dimensionality of PANAS negative emotions we proceeded with the exploration of the factors underlying negative emotions (n = 10 items). The number of factor to extract was determined by comparing the goodness of fit indexes of the model composed by the three factors of positive emotions and, sequentially and separately, 1-factor, 2-factor, 3-factor, and 4-factor for the negative emotions (see table 1, p.211).

The 3-factor model was selected since the goodness of fit indexes of the 4-factor model were not significantly improved. Together with the positive emotions joy, interest, and activation (Egloff et al., 2003) we found three dimensions that were labeled distress, anger, and fearfulness (cf. Zevon & Tellegen, 1982) (see table 2, p. 211). Such a 6-factorial model was tested on the second sub-sample (n = 491) in order to verify its goodness of fit, which was confirmed (CFI/TLI .94/.92 RMSEA = .06, χ^2/df = 2.71; cf. table 2).

4.3.6.2 Confirmatory analysis of the latent dimensions of PANAS, IPANAT, and TAS-20

Following a stepwise approach, the goodness of fit of the latent dimensions was tested by including all the dimensions within the same CFA, in line with Anderson and Gerbing (1988), and Newcomb (1990), who recommended first to test the "measurement model," and then testing a "structural model." Hence, the dimensions included were namely of explicit emotions (PANAS, 6 latent dimensions), implicit emotions (IPANAT, 2 dimensions), alexithymia (TAS-20, 3 dimensions). The goodness of fit indexes were below the acceptable thresholds (CFI/TLI .88/.87, RMSEA = .06, $\chi^2/df = 2.64$); precisely, problems were found in the alexithymia sub-scale EOT, on which the variables' loading ranged from .08 to .63. Moreover, while the other two sub-dimensions DIF and DDF were highly correlated (polychoric coefficient =.63, p<.001), EOT was poorly correlated with DIF (polychoric coefficient = .30, p < .001), but highly with DDF (polychoric coefficient = .52, p < .001). Based on these results and on the literature about TAS-20 that indicate EOT to be poorly reliable (e.g., de Timary, Roy, Luminet, Fillee, & Mikolajczak, 2008; Parker et al., 2003; Säkkinen, Kaltiala-Heino, Ranta, Haataja, & Joukamaa, 2007) and alexithymia to be still adequately captured by DIF and DDF (Haviland, Shaw, Cummings, & MacMurray, 1988), we decided to exclude EOT from the analysis to avoid misleading results. The goodness of fit resulted effectively improved (CFI/TLI .92/.90, RMSEA = .04, $\chi^2/df = 2.62$) and the loadings of explicit emotions ranged from .46 to 89 and all factors resulted with good reliability, namely joy ($\alpha = .69$), attentive ($\alpha = .65$), interest ($\alpha = .72$), distress (this factor was composed of 2 items, thus we computer the Pearson's $r = .61$, $p < .001$), anger ($\alpha = .72$), and fearfulness ($\alpha = .73$). The loadings of the implicit factors ranged from .75 to 86 and Cronbach's alphas resulted greater than

.80; the DIF factor showed loadings from .41 to .76 whereas the DDF resulted with loading from .50 to .90 and the Cronbach's alpha was greater than .80.

4.3.6.3 *Relationship between explicit and implicit emotions, and alexithymia*

Then, we proceeded by testing the association between explicit and implicit negative and positive emotions, and their relationship with the two dimensions of TAS-20. To improve the readability of the graphical representation of the model, two figures of the same model have been built: the figure 1 includes the associations between DIF and DDF, and with implicit emotions; within the same figure there were represented the association of implicit emotions with positive and negative explicit emotions. On the figure 2 (p. 212), the relationships between DIF and DDF, and positive and negative explicit emotions have been graphically represented; the implicit emotions have been graphically omitted, but were included in the SEM performed.

Positive implicit emotions resulted associated with greater positive explicit emotions and only with lower anger; likewise, negative implicit emotions resulted associated only with anger. The emotions assessed implicitly were highly correlated but showed different patterns of association with explicit emotions: the two dimensions of TAS-20, difficulties with identifying emotions and describing emotions, were differently associated with implicit emotions (figure 1) and explicit emotions (figure 2, p. 212). Overall, the pattern individuated suggests that the individuals who were unable to identify their emotions tended to experience more implicit and explicit negative emotions. The individuals who were unable to describe feelings reported less explicit emotions, in general, positive and negative, and less implicit positive emotions.

Study 2

4.3.7 Method

4.3.7.1 Participants and procedure

The participants (N = 158) were Italian HIV-positive men (84.81%) and women (14.56%) with a mean age of 40.25 (*SD*= 9.39) years. Participants' education included elementary school (1.27%), junior high school (4.43%), high school diploma (51.90%), university degree (9.49%), master's degree (17.09%) and Ph.D. or other specialization (6.33 %; missing data 9.49 %). Of the total sample, 75.32 % were treated with ART, whereas 22.15 % were naïve to ART (data missing 2.53 %).

Participants were recruited through a web-based non-probabilistic convenience sampling technique; recruitment took place over 11 months (from September 2010 to August 2011). They were invited to join the study through a message posted on web-site and forums related to HIV/AIDS, and the following information was provided to them, the general aims and description of the study, the inclusion criteria (HIV diagnosis and age over 18), and the name and last name, and affiliation of the investigators. Participants completed and submitted the questionnaires online, which were received electronically to an ad-hoc e-mail account built for this study. Participants' privacy and anonymity were constantly ensured and respected; participants were informed that the participation to the survey was voluntary, and they self-declared that were over 18 years of age.

Instruments

Similarly to study 1, explicit emotions were assessed with PANAS (Watson et al., 1988) whereas Implicit Positive And Negative Affect Test (IPANAT; Quirin et al.,

2009) was used to assess implicit emotions and alexithymia was assessed with the Toronto Alexithymia Scale (TAS-20; Bagby et al., 1994) (cf. study 1).

HIV progression biomarkers were self-reported and based on patients' latest analysis. CD4+ cells count is expressed as cells/L; viremia was expressed as plasma concentration of virus in copies/ml. Patients also self-reported whether they were currently treated with ART (coded as 1) or whether they were naïve to ART (coded as 2).

4.3.7.2 Data Analysis

The analyses were performed with SPSS 15.0 (SPSS Inc. Chicago, IL, 2006) and Mplus 6.1 (Muthén & Muthén, 2010); the first one was used to calculate skewness and kurtosis that assess variables' distributions (if lower than |1| were treated as normally distributed, if greater than |1| were treated as non-normally distributed). Mplus 6.1 was used to perform the SEM (Structural Equations Modeling) to test the associations between the negative and positive emotions (implicit and explicit), alexithymia dimensions, and the biomarkers of HIV progression. The Weighted Least Square Method (WLSM) was used since few variables violated the assumption of normal distribution. The Goodness-of-fit indexes adopted were the Tucker-Lewis Incremental fit index (TLI; Tucker & Lewis, 1973), the Comparative Fit Index (CFI; Bentler, 1990), RMSEA and the χ^2/df ratio (Crowley & Fan, 1997). CFI and TLI scores ≥ .95 indicated good fit, while scores ≥ .90 indicated sufficient fit. A RMSEA score ≤ .05 indicated a good fit, whereas a score ≤ .08 indicated a sufficient fit of the model. A χ^2/df ratio ≤ 5 indicated a good fit for the model (Bollen, 1989; Crowley & Fan, 1997; Hu & Bentler, 1999; Schermelleh-Engel et al., 2003).

Student's t test was used to compare the sample of HIV-positive individuals with the sample of HIV-negative individuals respect to the two dimensions of alexithymia.

4.3.8 Results

4.3.8.1 Confirmatory analysis of the latent dimensions of PANAS, IPANAT, and TAS-20

First, the latent dimensions were tested and resulted with an adequate fit (CFI/TLI .93/.92, RMSEA = .04, $\chi^2/df = 1.31$). The loadings of explicit emotions ranged from .49 to .93 and the dimensions showed adequate reliability (Cronbach's alpha greater than .72; the two items of *distress* resulted were correlated $r = .66$, $p < .001$). The loadings of the implicit factors ranged from .69 to .99 and the Cronbach's alpha was greater than .83. The DIF factor showed loadings from .53 to .83, whereas the DDF resulted with loadings from .32 to .93; their reliability was good with alpha greater than .75.

4.3.8.2 Relationship between explicit and implicit emotions, and alexithymia

The relationships between explicit and implicit emotions were tested, together with their association with two factors of TAS-20; then, it has been tested whether such emotions-related factors were associated with the two HIV progression biomarkers viral load and CD4+ cells count. The figure 3 includes the associations between DIF and DDF, and with implicit emotions; in the same figure there were represented the correlations of implicit emotions with positive and negative explicit emotions, and only the significant associations of the latent dimensions with HIV progression biomarkers have been represented. On the figure 4, the relationships between DIF and DDF and positive and negative explicit emotions have been illustrated and, as in the study 1, the implicit emotions have been omitted within the graphic

representation in order to improve readability; nonetheless, the two figures refer to the same single SEM performed.

As showed in figure 3, difficulties in identifying feelings was associated with greater negative implicit emotions, whereas difficulties in describing feeling was not associated with positive or negative implicit emotions; the latters, showed both coherent associations with explicit emotions, except for attentive dimension. The relationships with HIV biomarkers (CD4+ cells count and viral load) were instead limited to two discrete negative emotions (figure 4), namely greater fearfulness was associated with greater viral load and greater anger was associated with greater CD4+ cells count. Viral load predicted lower CD4+ cells count and participants who were not treated with HAART (1=treated, & 2=naïve) resulted with greater viral load.

With respect to the association between DIF and DDF (figure 4) it should be noted that the difficulties in identifying emotions was related to greater negative explicit emotions and lower positive emotions. The dimension Difficulties in describing feelings, instead, was associated with lower interest, attentive dimensions (positive explicit) as well as with lower distress. A single indirect relationship was significant, the one of negative implicit emotions on CD4+ cells count through anger ($\beta = -.10$, $p = .01$). As a last test, we verified whether the scores of DDF and DIF differed between the two groups, and the results indicated that HIV positive individuals scored higher on DIF ($t = -2.80$, $p = .005$; mean difference = -1.53) whereas no difference has been found on DDF ($t = 1.24$, $p = .22$).

4.3.9 Discussion

In this work, we investigated the dimensionality of emotions explicitly assessed and tested their association with the emotion implicitly assessed, as well as with alexithymia; furthermore, we also evaluated the relationships between such emotions-related dimensions with HIV-progression biomarkers such as CD4+ cells count and viral load on a sample of HIV-positive individuals. Emotions are undoubtedly important as risk as well as protection factors on individuals' health, and the presence of alexithymia may further threatens individuals' well-being (e.g., Carré et al. 2011; Evren et al., 2008; Hendryx, Haviland, & Shaw, 1991; Parker, Taylor, & Bagby, 2003; Rose, & Segrist, 2012). Emotions, which can be conceptualized as negative, neutral, or positive (valence) and on the basis of the arousal produced by them (Viinikainen et al., 2010), are quite often assessed with PANAS (Watson et al., 1988) a psychometric instrument that provides scores of negative and positive emotions. However, this bi-dimensional categorization may be too restrictive although extremely useful; emotions, indeed, could be rather assessed hierarchically (e.g., Mehrabian, 1998) and the bi-dimensionality "positive/negative" may represent the two second-order factors. In line with Egloff et al. (2003; see also Zevon & Tellegen, 1982) we found that emotions may be better explained with a more complex categorization considering different positive and negative discrete emotions. In fact, six dimensions were found and accordingly labeled as joy, attentive, interest (Egloff et al., 2003), distress, anger and fearfulness (e.g., Zevon & Tellegen, 1982). Our results are in line with Mehrabian (1998), and Egloff et al. (2003) that suggested a more complex structure of PANAS; furthermore, the significance of assessing emotions explicitly or indirectly/implicitly (e.g., Quirin et al., 2009) stems from the fact that not every individual may be capable to process emotional information and alexithymic individuals are emblematic for their cognitive impairment. Overall, we

found that implicit and explicit assessments of emotions are correlated but not overlapping, in fact, the associations found are significant but do not indicate collinearity. The major issue individuated in our studies, suggests that TAS-20 may be partially reliable and, in line with previous studies, only two of the three subscales (DIF and DDF) were confirmed, where EOT showed very poor internal consistency and low loadings (e.g., de Timary et al., 2008; Parker et al., 2003; Säkkinen et al., 2007). Interestingly, our investigations showed that the two alexithymia's sub-dimensions are highly correlated but may be differently associated with emotions. Namely, the difficulties with identifying emotions are associated with lower positive emotions but greater native emotions (Lumley et al., 1996; Palmer et al., 2002) whereas the difficulties with describing emotions, which consists in the difficulties with verbalizing one's emotions, resulted inversely associated with negative and positive explicit emotions. This may mean that individuals unable to describe their emotions may fail to report either negative or positive emotions. Furthermore, the difficulties with identifying emotions showed correlations of greater magnitude on negative emotions, in line with the literature. However, future investigation will help to clarify the different action of these two dimensions of alexithymia.

Lastly, we tested if there was a relationship between emotions (assessed implicitly and explicitly) and the two dimensions of alexithymia and the biomarkers of HIV progression.

Anger effectively correlates with lower CD4+ T-cells count whereas fearfulness correlates with greater viral load, although we cannot draw any conclusion or directionality respect to these relationships, we cautiously suggest explanations based on the literature that showed negative emotions to be associated with greater viremia (Kalichman et al., 2002). More precisely, lower CD4+ cells count was associated with anger, which was composed of emotions such as hostile, irritable, nervous, and jittery

in line with Cole and colleagues (2003; see also Leserman et al., 2002) who found irritability and hostility to be associated with a faster progression of HIV. Likewise, fearfulness composed of guilty, scared, ashamed, and afraid resulted associated with greater viremia, in line with Dickerson et al. (2004) who suggested that emotions that threaten the self might lead to faster HIV progression. Nonetheless, the behavioral pathway should not be neglected, as negative emotions may lead to more dysfunctional coping such as alcohol use (Buchmann et al., 2010; Cooper et al., 1995; Pardini et al., 2004) or poorest adherence to HAART (Power et al, 2003). Besides, the physiological and behavioral pathways may interact together in determining HIV progression.

Taken together, our results provide support about the utility of adopting both explicit and implicit assessment of emotions and prudently, we would suggest that within the category of negative emotions there might be certain emotions that are more influential on health than others. Likewise, the construct of alexithymia proven to be significantly and peculiarly associated with positive and negative emotions implicitly and explicitly assessed.

4.3.10 Limitations

This work may possess limitations that need to be overcome in order to provide more precise results; first of all the cross-sectional nature of the studies limit the conclusions drawn since no directionality can be stated. Furthermore, the two samples were recruited with convenience technique; thus, there is limitation on the degree of results' generalizability. Despite the limitations, our results are in line with previous studies conducted; furthermore, we currently concluded a longitudinal study through which we will evaluate the effect of emotions and alexithymia longitudinally on a sample of HIV-positive individuals.

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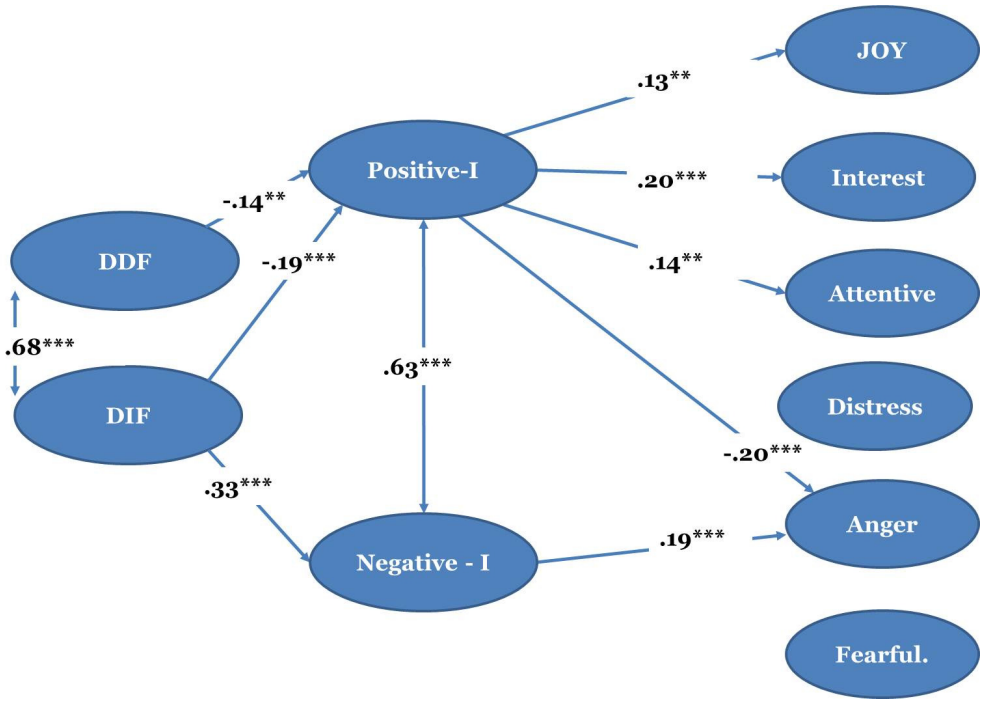
Table 1 Comparison of the 4 factorial solutions' goodness of fit indexes (PANAS)

Model	CFI	TLI	RMSEA	χ^2/df
1-factor	.880	.861	.077	3.92
2-factor	.923	.909	.063	2.92
3-factor	.937	.915	.060	2.78
4-factor	.943	.918	.059	2.73

Table 2 Six-factor model and items' loadings obtained on two samples

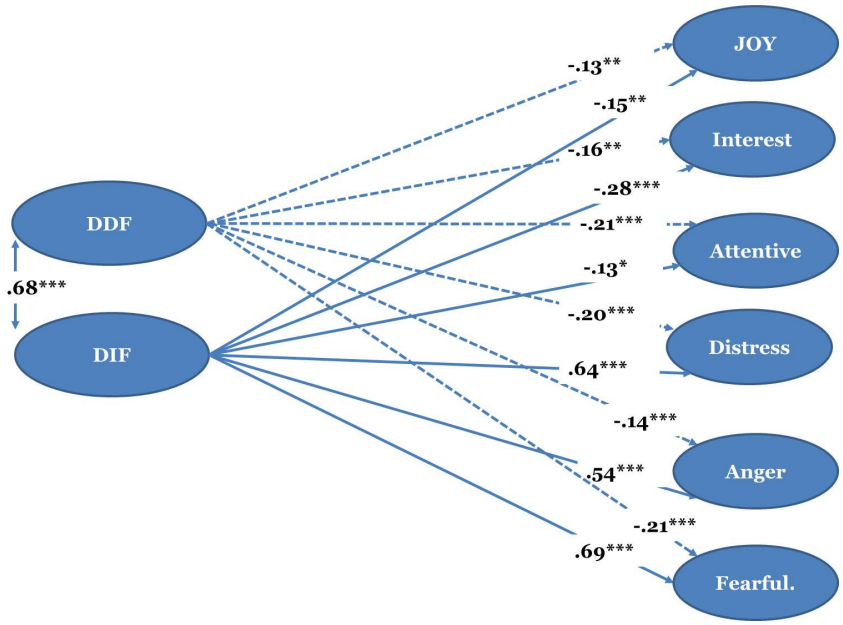
		Sample 1	Sample 2
Dimension	**Item**	**Loading**	**Loading**
Joy	Excited	.523	.520
	Enthusiastic	.876	.855
	Proud	.554	.630
Attentive	Alert	.545	.560
	Inspired	.623	.583
	Attentive	.604	.629
	Active	.669	.773
Interest	Interested	.509	.473
	Strong	.599	.747
	Determined	.685	.689
Distress	Distressed	.500	.883
	Upset	.403	.781
Anger	Hostile	.616	.789
	Irritable	.878	.915
	Nervous	.894	.494
	Jittery	.522	.667
Fear	Guilty	.374	.583
	Scared	.778	.926
	Ashamed	.628	.519
	Afraid	.943	.860

Figure 1 Association between DIF and DDF and implicit emotions, and implicit emotions with explicit emotions



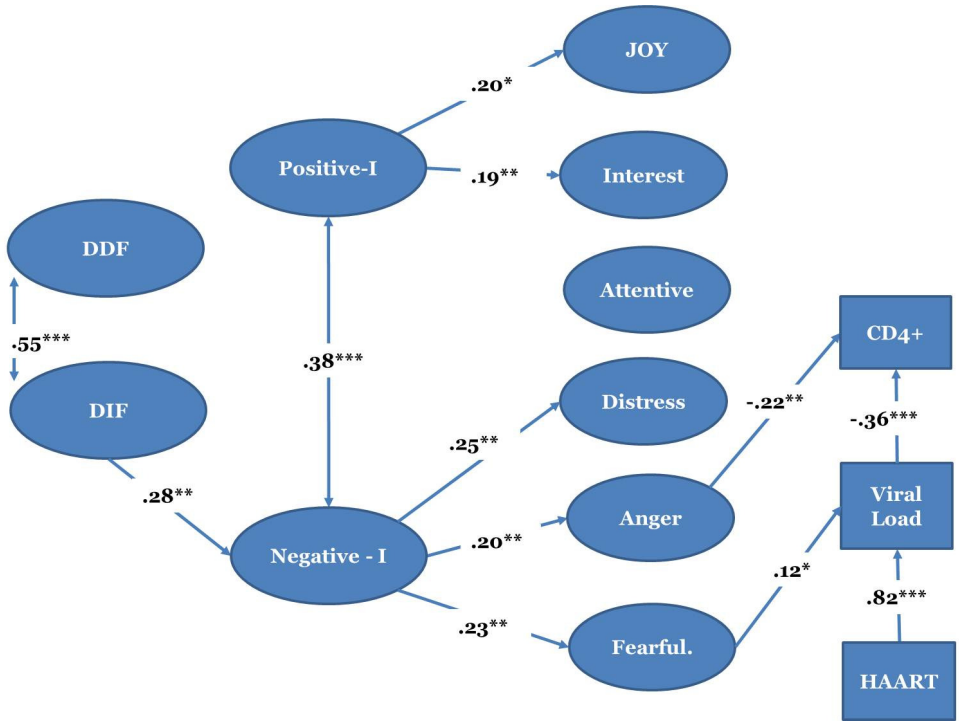
** p < .05, ** p < .01, *** p < .001*

Figure 2 Association bewteen DIF and DDF and explicit emotions, without the graphical representation of the implicit emotions



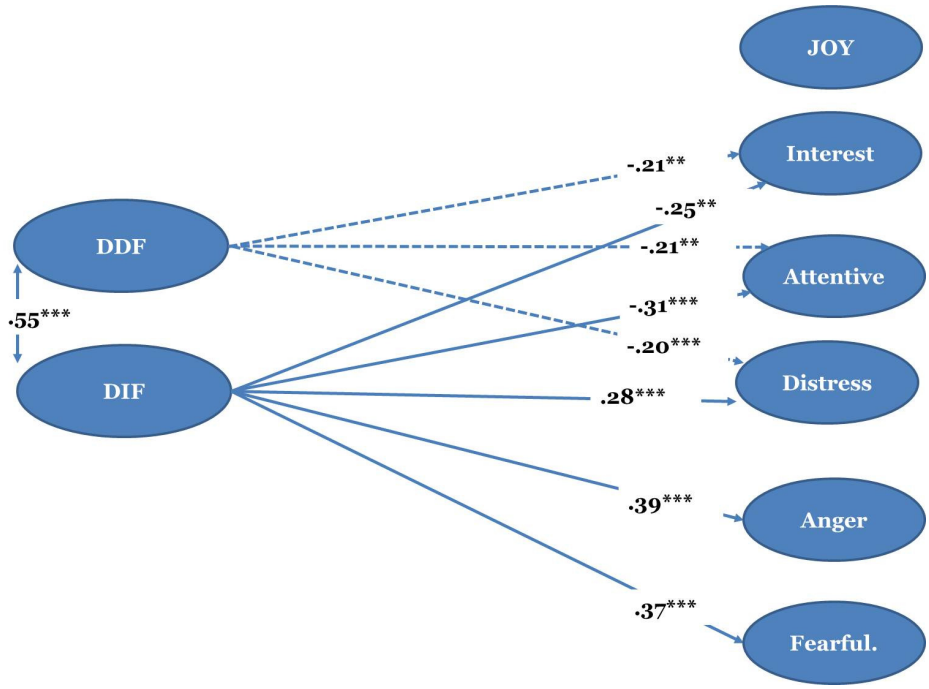
** p < .05, ** p < .01, *** p < .001*

Figure 3 Association between DIF and DDF and implicit emotions; implicit emotions with explicit emotions, and HIV progression biomarkers



** p < .05, ** p < .01, *** p < .001*

Figure 4 Association of DIF and DDF with explicit emotions without the graphical representation of implicit emotions.



** p < .05, ** p < .01, *** p < .001*

4.4 How can we predict the risk for disease? Personality profiles and their characteristic patterns of emotions and coping strategies might predict depression

Norcini Pala, A., & Steca, P.

Abstract

Individual differences may be either protective or risk factors for one's mental health, especially considering negative emotions versus positive emotions, and unhealthy versus healthy coping strategies. Personality traits can help to predict such individual differences, e.g., respect to the tendency to experience greater negative emotions and to engage in unhealthy coping strategies. The "functional/dysfunctional" patterns (e.g., positive emotions and functional coping vs. negative emotions and dysfunctional coping) may ultimately predict the risk of depression. This work is focused on personality prototype and their relationships with emotions, and coping strategies, linking them to the risk of depression. A large sample of individuals (N = 955) has been recruited and each participant compiled a battery of questionnaires that assessed personality, emotions, coping strategies and depression. In line with the specific literature, three clusters of individuals who differed on the five dimensions of personality have been identified and accordingly labeled resilient, and overcontrolled, with a slightly modified cluster named as "emotionally stable." The discriminant analysis showed that two big personality factors called *plasticity* and *stability,* essentially helped to discriminate among the clusters. The profile "overcontrolled" was characterized with lower stability and moderately high plasticity; the cluster "emotionally stable" was characterized with lower plasticity and moderately high stability. Lastly, the cluster "resilient" was characterized with greater plasticity and stability. With respect to clusters' patterns of emotions and coping strategies, we found that overcontrolled scored higher on negative than positive emotions; emotionally stable individuals were characterized with moderately high positive and negative emotions. Resilient scored higher on positive emotions, and lower on negative emotions and were very likely to engage in functional coping. In opposite, overcontrolled individuals were more likely to engage in dysfunctional coping and

were at greater risk for depression. Taken together this may suggest that resilient profile and, in part, emotionally stable may have protective aspects that prevent the development of depression.

Key words: Personality prototypes; Emotions; Coping; Depression;

4.4.1 Introduction

Certain individuals are more vulnerable than other to mental illness and their psychological features can be extremely useful to predict such a risk. Personality traits may be extremely informative also for their genetic characteristics (see (Jang et al., 2006) and genetic connection with depression (Kendler & Myers, 2010). Personality traits are generally defined as stable over time, and this also allows a longitudinal prediction of, e.g., behaviors; thus, for instance, in the context of chronic illness care, clinicians might target the individuals who are at greater risk for depression, acting in order to prevent the occurrence of mental disorders or unhealthy behaviors, both of which may impair patients' health (e.g., Rabkin, 2008). Support to the assumption of personality traits in determining mental health can be drawn by Friedman (2007; Kern & Friedman, 2008) who claimed personality traits to interact dynamically in promoting health, explaining why some individuals are more prone than others to get sick (Friedman, 2008). Configurations of personality traits, however, may be more informative than the single traits, in understanding the relationships with mental health; namely, the person-centered approach, which focuses on individuals' peculiar characteristics and their organization might add to the information deriving from the "variable-centered" approach (Steca, Alessandri, & Caprara, 2010).

One of the most widely adopted model of personality is the Big Five (Costa & McCrae, 1996) that assesses individuals' differences in terms of five dimensions, namely Neuroticism (N or Emotional Stability), Extraversion (E), Openness to Experience (O), Agreeableness (A), and Conscientiousness (C). Such traits are associated with mental health and more precisely neuroticism is essentially the most significant predictor for depressive symptoms and substance use (Joseph & Wood, 2010; Kotov,

Gamez, Schmidt, & Watson, 2010; see also Kendler & Myers, 2010). Focusing on the configuration of personality traits derived from the person-centered approach, there is substantial support about the existence of three profile which have been labeled undercontrolled, overcontrolled, and resilient (Berry, Elliott, & Rivera, 2007; Steca et al., 2010). These clusters have been associated with adaptive and maladaptive personal characteristics and behaviors, as well as with positive and negative life outcomes (cf. Asendorpf, Borkenau, Ostendorf, & Van Aken, 2001; Hart, Atkins, Fegley, Robins, & Tracy, 2003; Robins, John, Caspi, Moffitt, & Stouthamer-Loeber, 1996; Steca et al., 2010; Steca, Alessandri, Vecchio, & Caprara, 2007). Therefore, they may be useful for researchers that aim to identify proneness to health or conversely illness, also considering emotions and coping strategies as part of the path through which mental illness might be exacerbated. Accordingly, as we were interested in individuating individual resources (e.g., functional coping and positive emotions) that may be associated with lower risk of depression, we adopted the person-centered approach in order to identify resources and risk factors associated with personality profile, and ultimately with risk for depression.

4.4.1.1 Personality and emotions

Emotions represent risk or protective factors for one's well-being. (Fredrickson & Joiner, 2002), for instance, have claimed that positive emotions produce an upward spiral toward enhanced emotional well-being. Interestingly, positive emotions, and happiness specifically might produce favorable changes in one's life also supporting the development of resources for living well (Cohn, Fredrickson, Brown, Mikels, & Conway, 2009). Furthermore, there is clear evidence of the relationship between

positive emotions and physical health (Brummett, Boyle, Kuhn, Siegler, & Williams, 2009; Kreibig, 2010; Lane, Reis, Peterson, Zareba, & Moss, 2009). Whereas, negative emotions have been associated with impairments of the immune system functioning (Cole, 2008), as well as with unhealthy behaviors such as alcohol use (e.g., Buchmann et al., 2010; Pardini, Lochman, & Wells, 2004). Thus, emotions are substantially individuals' resources to which one can draw to face with adversities, and may prevent the development of depression ultimately.

Emotions, however, are strictly related to personality traits (Yik & Russell, 2001) as for instance, neuroticism correlates with anxiety, fear, guilt, self-disgust, and shame whereas conscientiousness, extraversion, and openness correlate with positive emotions. More precisely, conscientiousness correlates with happiness, hope, and pride; extraversion has been found to correlate with happiness and pride, and agreeableness with happiness. Lastly, openness is associated with lower shame and fear (see Penley & Tomaka, 2002). Furthermore, in line with the person-centered approach, there are studies supporting that the individuals who belong to the prototype of resilient and undercontrolled ted to score higher on positive emotions (e.g., Steca et al., 2010; Gramzow et al., 2004) discussed the three prototypes with respect to emotions, defining undercontrollers as able to express emotions immediately and directly and to be more spontaneous and approach oriented but still distractible and impulsive. Moreover, they may be characterized with fluctuating emotions (Block, 2002; Funder & Block, 1989). Oppositely, those considered overcontrollers tend to be rather inhibit about emotions and may be more avoidant and intolerant of ambiguity, and more rigid, in the end. Thus, accordingly to the personality typology frame, we would understand whether personality and emotions might interact in favoring mental well-being, namely reducing the risk of depression.

4.4.1.2 Personality and coping strategies

Personality traits are also associated with coping strategies (e.g., Carver & Connor-Smith, 2010). Nevertheless, there are many ways to cope with stressors, coping strategies can be defined as functional (adaptive) of dysfunctional (maladaptive) where in the first category there are, e.g., problem-focused coping, seeking of social support whereas within the category of dysfunctional coping one may find emotional discharge and disengagement (e.g., Scheier, Weintraub, & Carver, 1986).

As regards correlations with personality traits, Neuroticism has been associated with emotion-focused strategies, namely the strategies adopted to reduce the negative emotional arousal (Lazarus & Folkman, 1984a, 1984b). Likewise, individuals high on neuroticism are less likely to engage in problem-focused coping, namely the strategies aimed to remove or to solve the cause(s) of stressful events (Hooker, Monahan, Bowman, Frazier, & Shifren, 1998; McCrae & Costa, 2006; Watson & Hubbard, 2006). Individuals high on neuroticism may be more prone to avoidance also for the greater negative emotions and distress experienced (McCrae & John, 1992; Miles & Hempel, 2003); furthermore, negative affect might make hard to engage in cognitive restructuring (Carver & Connor-Smith, 2010). Extraversion, instead, predicts the adoption of problem-focused strategies (McCrae & Costa 2006; Watson & Hubbard, 2006) and it has been negatively associated with emotion-focused coping (O'Brien & DeLongis, 1996). Extraversion, involves greater positive emotions, sociability, assertiveness, and high energy (e.g., Caspi, Roberts, & Shiner, 2005) that together may lead to greater likelihood to engage in problem focused coping cognitive restructuring and social support coping (e.g., Carver & Connor-Smith, 2010). Conscientiousness, which implies persistence, greater organization, and achievement orientation (McCrae & John, 1992) may promote the adoption of

problem focused strategies and less likely the adoption of disengagement (e.g., Vollrath, 2001). Agreeableness that is characterized with high levels of trust and concern for others (McCrae & John 1992) and stronger social relationships (Bowling, Beehr, & Swader, 2005) may increase the likelihood of engaging in social support coping. Moreover, openness might be associated with emotion-focused strategies such as hostile reaction, sedation, and reappraisal (McCrae & Costa, 2006). However, for the features of imagination, creativeness and curiosity (McCrae & John, 1992), and individuals characterized with this trait may be very likely to engage in cognitive restructuring and disengagement such as wishful thinking (see for instance, Carver & Connor-Smith, 2010).

In line with the literature about typologies, we might hypothesize overcontrollers to be more avoidant and to engage in dysfunctional coping (Block, 2002; Funder & Block, 1989). Whereas, resilient individuals are expected to engage in functional coping also considering that those who experience greater positive emotions tend to adopt functional coping strategies (Cohn et al., 2009); these characteristics may predict than lower risk of depression (Greenglass & Fiksenbaum, 2009). Hence, based on personality traits and for their significant associations, there may be individuals that more likely than others engage in functional or dysfunctional coping strategies.

4.4.1.3 Aims

Our aim was to verify whether through the person-centered approach we were able to identify prototypes of individuals that based on their personality traits, and then on emotions and coping strategies were differently at risk for depression. More precisely,

the aim of this work was to verify the reproducibility of the three clusters referred to the five dimensions of the Big Five model in a prospective of person-centered approach, and we were interested in verifying whether these three prototypes could differentiate individuals in term of emotions (positive/negative), coping strategies, and ultimately in risk of depression. We expected to observe greater positive emotions (Steca et al., 2010) and lower depression risk among resilient and undercontrolled in line with Berry et al. (2007) for resilient and undercontrollers than overcontrollers. Functional coping strategies were expected more frequent on resilient and undercontrollers, than in overcontrolled (e.g., Berry et al., 2007).

4.4.2 Method

4.4.2.1 Participants and procedure

The participants (N = 955) were men (48.48 %) and women (50.99%; data missing .53%) and their mean age was 29.51 years (SD = 6.71) and their education included junior high school (5.34%), high school diploma (53.50%), university degree (19.69%), master's degree (17.49%) and Ph.D. or other specialization (2.83%; data missing 1.15%).

Participants have been recruited with the snowballing sampling technique by students of the course of "emotion and motivation" of Milano-Bicocca University, who received 2 extra points on their final grade. Students were instructed to recruit 50% of men and 50% women, none of which should have been of their closest family (e.g., relatives or parents), in order to reduce social desirability. All participants completed and submitted a battery of questionnaires through Internet and self-declared to be over 18 years old.

4.4.2.2 Instruments

Personality traits were assessed through the short form of the Big Five Questionnaire (BFQ; Caprara, Barbaranelli, Borgogni, & Perugini, 1993), which consisted in 60 items relative to the 5 traits and their 10 facets. Each facets was composed of 6 items that respondents scored on a 5-point scale ranging from complete disagreement (1 = *Very false for me*) to complete agreement (5 = *Very true for me*) to rate the extent to which each item described them. The dimensions assessed were Energy (E) that refers to Extraversion (McCrae & Costa, 1987), and is organized into the two facets "Dynamism" (expansiveness and enthusiasm), and "Dominance" (assertiveness and confidence). Openness (O), organized into the two facets "Openness to Culture" (essentially referred to the broadness or narrowness of one's own cultural interests) and "Openness to Experiences" (e.g., openness to novelty, interest toward different people, habits and life-styles). Agreeableness (A), which is organized into the facets "Cooperativeness/Empathy", (concern and sensitiveness towards others and their needs) and "Politeness", (kindness, civility, docility and trust). Emotional Stability (ES) that refers to Neuroticism and consists in two facets, namely "Emotion Control" (the capacity to cope adequately with one's emotionality) and "Impulse Control" (the capability of controlling irritation, discontent, and anger). Conscientiousness (C) instead is organized into two facets, "Scrupulousness" (e.g., orderliness and precision) and "Perseverance" (the capability of fulfilling one's own tasks and commitments; Caprara et al., 1993). The Cronbach's alpha of the five domains ranged from .71 to .87 indicating good reliability (the variables were all normally distributed therefore there was no need to calculated the theta coefficient).

Depression was assessed with the Patient Health Questionnaire (PHQ-9; Kroenke, Spitzer, & Williams, 2001) that consists in 10 items referred to the diagnostic criteria of depression of which participants rated the frequency during prior 2 weeks from 0 (*Not at all*) to 3 (*Nearly every day*). Few variables departed from the normal distribution so both alpha and theta coefficients were calculated, showing a very good reliability of the instrument (α = .80 and θ = .81), and for this study the items were summed into an "overall" score of depression.

Positive and negative emotions were assessed with the Positive-And-Negative-Affect-Schedule (PANAS; Watson, Clark, & Tellegen, 1988). Participants rated each of the 20 emotions listed using a Likert scale from 1 (*Very slightly or not at all*) to 5 (*Extremely*). The dimensions of PANAS assessed in this work were those found by Norcini Pala and Steca (unpublished manuscript) and consisted in 6 first-order dimensions (discrete emotions) Joy, Attentive, Interest (Egloff, Schmukle, Burns, Kohlmann, & Hock, 2003), Distress, Anger and Fearfulness (e.g., Zevon & Tellegen, 1982) underling two second order factors "positive" and "negative" emotions (cf. Mehrabian, 1995). The Cronbach's alpha of the dimensions related to positive emotions indicated sufficient reliability: joy (α = .69), attentive (α = .65), interest (α = .72). The negative emotions items departed from the normal distribution (skewness and/or kurtosis greater than |1|) thus both alpha and theta (a coefficient that performs better than Cronbach's alpha in case of non-normal distribution; see Zumbo, Gadermann, & Zeisser, 2007), were computed. The dimension "Distress" was composed of two items, therefore Spearman r was computed (r_s = .61), anger (α =.72, and θ = .79), and fearfulness (α = .73, and θ = .79). The coefficients indicated adequate reliability of the factors.

Coping strategies were assessed with 14 items designed on the brief cope by Carver, Scheier, and Weintraub (1989). The items were built to assess active coping (e.g., *I've been taking action to try to make the situation better*), seeking social support (e.g., *I've been seeking for support from others*), passive coping (e.g., *I admitted I cannot deal with the situation and gave up attempting to cope with it*), religious coping (*I've been trying to find comfort in my religion*), humor coping (*I've been making jokes about my problems*), alcohol use (*I drink alcohol to make myself feel better*), and re-appraisal (e.g., *I've been trying to see it in a different light, to make it seem more positive*). The participants rated these items on a Likert-type scale ranging from 1 (*Never*) to 4 (*Very often*). This questionnaire was built ad-hoc by our research group, no references on the instrument's structure of psychometric properties were available, and therefore in this paper we explored the dimensionality of the instrument. Although it was based on the COPE by Carver et al. (1989) no a priori dimensionality was definable also for the controversies about COPE dimensionality (cf. for instance Snell, Siegert, Hay-Smith, & Surgenor, 2011, and Pang, Strodl, & Oei, 2012), therefore an exploratory approach seemed more appropriate.

4.4.2.3 Data analysis

SPSS 20 (Statistical Package for the Social Sciences, Chicago, IL) and Mplus 6.1 (Muthén & Muthén, 2010) were used to perform the analyses. Skewness and kurtosis were computed to assess the distribution of variables; factors reliability was assessed with Cronbach's alpha when all items were normally distributed and theta coefficient if *all* or *some* items were non-normally distributed (see Zumbo et al., 2007). In fact, alpha coefficient is negatively influenced by departure from normality of items.

The cluster analysis was performed to form an empirical classification of the participants based on their scores on the dimensions of Big Five. More precisely, we used the two-step clustering analysis approach that automatically determined the number of clusters to form, based on clusters' Euclidean distance, and Schwarz's Bayesian inference criterion (BIC). This approach included in SPSS performs very good especially when all the variables are normally distributed (Bacher, Wenzig, & Vogler, 2004).

Then, the discriminant analysis was performed in order to individuate the discriminant functions (linear combinations of the 5 traits) that maximally discriminate between the clusters extracted. The method used was the stepwise with the Wilk's Lambda criterion, and the coefficients were rotated (varimax) (see Barbaranelli, 2006). Box test was used to test homogeneity of variance (H_0 the variance are equal), eigenvalue indicates the proportion of variance explained, whereas Wilks's Lambda indicates the significance of the discriminant function.

The variables about coping strategies were factor analyzed with Mplus, using the WLSM extraction method, as the items were Likert-type scale (5-point) and some of them departed from normal distribution; the number of factors to extract was determined by the RMSEA threshold that should be lower than .05 (Browne & Cudeck, 1992). In this case, the Mplus 6.1 provided the factor determinacy by default; this coefficient assessed latent factors reliability taking into account variables' nature (e.g., ordinal non-normally distributed).

Then, ANOVAs were performed to test the clusters difference on depression, emotions, and coping strategies; the Tukey HSD post-hoc was used as it provided classification of clusters based on the significance of the post-hoc difference.

4.4.3 Results

4.4.3.1 *Two-step cluster analysis of the big five dimensions*

Through the two-step cluster analysis, three groups were obtained (BIC changes were: from 1 to 2 clusters -324.47; from 2 to 3 clusters -175.09; from 3 to 4 clusters -85.36; see table 1). The first cluster was characterized with all scores of each dimension below the average; the second cluster was characterized with higher emotion stability, and agreeableness slightly above the average. Energy and openness were extremely low, even more than cluster 1. Cluster three, was instead characterized with all scores above the mean, although emotion stability was lower than cluster two (cf. figure 1). Then, in order to individuate the linear combination (discriminant functions) of the five dimensions adopted in the cluster analysis, a discriminant analysis was conducted. Two functions were individuated (Box test = 175.11, F = 5.79, p = .001), the first one explained the greatest part of variance (67.50%; eigenvalue = 1.57) whereas the second one explained the 32.50% of variance (eigenvalue = .75) and resulted both significant (Lambda Wilks $p < .001$; cf. table 2). The clusters were compared with the three clusters previously identified on Italian samples by Steca et al. (2010) and Barbaranelli (2002), while our cluster 1 may generally identify the overcontrolled and cluster 3 recalls resilient, the cluster 2 actually differed from the cluster undercontrolled especially for the higher score on emotional stability (see figure 1; note: the labels used on the figure are not definitive, see below). Therefore, we proceeded confuting a discriminant analysis to further understand clusters' characteristics. The two functions identified overlap the 2 second order factors named Stability (Emotional Stability, Agreeableness, and Conscientiousness) and Plasticity (Extraversion and Openness) underlying the 5 dimensions of the Big Five (cf. DeYoung, Peterson, & Higgins, 2002). Therefore, we described the clusters accordingly, in fact based on the centroids difference respect

the discriminant function (see Table 2), the clusters resulted characterized with low stability and moderate plasticity (cluster 1 or "overcontrolled"), moderated stability and low plasticity (cluster 2 the supposed "undercontrolled"), high stability and plasticity (cluster 3 "resilient"). For the partial lack of fit of the clusters (compared to the three clusters described in the literature) as "emotionally stable" the group 2, for the higher score on emotional stability and above the average score on agreeableness. The cluster 1 was forcedly labeled overcontrolled, and cluster 3 resilient.

4.4.3.2 Differences among clusters on depression and emotions

ANOVAs were performed in order to evaluate the clusters' features respect to emotions and depression. Respect to emotions, overcontrolled and emotionally stable were characterized with greater negative emotions respect to resilient, which together with emotionally stable scored significantly higher than overcontrolled on positive emotions (Table 3). Hence, "resilient" was characterized with greater positive emotions and lower negative emotions; "overcontrolled" was characterized with lower negative emotions and greater positive emotions. "Emotionally stable" showed greater negative emotions than resilient, but not greater than overcontrolled; conversely, positive emotions were higher on emotionally stable than overcontrolled but no difference was observed between emotionally stable and resilient. Therefore, we hypothesize emotionally stable to be characterized, indeed, with "balanced" or fluctuant emotions (cf. Block, 2002; Funder & Block, 1989). Lastly, overcontrolled scored higher on depression respect to emotionally stable and resilient ($F = 43.79$, $p < .001$; HSD Tukey post-hoc $p < .001$: $M_{2,3} = 5.23$ and 5.81, $M_1 = 8.61$).

4.4.3.3 Coping strategies

The 14 items used to assess coping strategies were factor analyzed with Mplus 6.1 using WLSM extraction method and the promax rotation; the 5-factor solution resulted barely acceptable with RMSEA = .056. However, one item (*I drink alcohol to make myself feel better*) did not show any loading greater than .30 on the factors, and the items "*I've been trying to find comfort in my religion*" resulted the only item loading on a factor. Furthermore, the factors interpretability was not fully satisfying. Thereby, these two items were excluded and another EFA was performed; the 5–factor solution resulted now extremely good (RMSEA = .029) and the factors interpretability was significantly improved (see table 4). Mplus 6.1 provided, by default, the *factor determinacy*, a reliability coefficient that evaluates reliability on the basis of the correlation between the item and the latent dimension. The coefficients ranged from .77 to .99, indicating optimal reliability of the factors. In this case, we did not computed alpha (or Spearman's r) or theta coefficient since the factor determinacy was calculated taking into account the variables' distribution. The factors extracted were labeled as (1) active coping (2 items; e.g., *I've been taking action to try to make the situation better*), (2) seeking social support (2 items; e.g., *I've been seeking for support from others*), (3) passive coping (3 items; e.g., *I admitted I cannot deal with the situation and gave up attempting to cope with it*), (4) re-appraisal (3 items; e.g., *I've been trying to see it in a different light, to make it seem more positive*), and (5) avoidance (2 items; e.g., *I acted as if nothing had ever happened to me*). The two items excluded were retained and considered as proxies of alcohol use "*I drink alcohol to make myself feel better"* and religious coping "*I've been trying to find comfort in my religion"*. This interpretation was partially supported by Pang and colleagues (2012) and O'Donnell and colleagues (2008).

4.4.4 *Differences among clusters on coping strategies*

The ANOVA was performed in order to test the differences between clusters about the coping strategies; the results listed on table 9 showed significant differences. The overcontrolled and emotionally stable scored higher on avoidance, and lower on active respect to cluster resilient; only overcontrolled scored lower on religious coping respect to cluster resilient. The individuals in the cluster overcontrolled, tended to use alcohol to reduce distress, and to adopt a passive coping more than emotionally stable and resilient. Emotionally stable, and resilient, in their turn, scored higher on re-appraisal than overcontrolled. The seeking social support resulted less engaged by overcontrolled and more by resilient, whereas emotionally stable did not show significant difference (cf. table 5).

4.4.5 Discussion

There is accord in stating that some individuals are more prone than others to get sick and to develop mental disorder such as depression (e.g., Friedman, 2007; Kern & Friedman, 2008); well-being must be seen as a dynamic movement that goes from "ill health" (dis-ease) to "total health" (ease) (cf. Antonovsky, 1979), and individuals may use their resources in order to prevent unfavorable outcome. The personality typology may explain this trend and can help us to predict or individuate who is at greater risk for depression. In fact, there is evidence of the utility and feasibility of the personality clusters identified here as resilient, emotionally stable, and overcontrolled, where the first two groups are at lower risk to develop depression (Berry et al., 2007) and to experience positive emotions (Steca et al., 2010).

Although the differences observed in our clusters respect to the clusters discussed in the literature, we compared and interpreted our results in line with the literature. We confirmed both aspects as positive emotions were significantly more reported by individuals in resilient and emotionally stable (referred to undercontrolled), which were actually less likely to score higher on depression. Interestingly, in part in line with Block (2002; Funder & Block, 1989), while overcontrolled individuals were strongly characterized with more negative emotions, and resilient individuals with positive emotions, emotionally stable showed a substantially "fluctuant" (as indicated by the authors) or more *balanced* emotionality. Likewise, while dysfunctional coping was ore pronouncedly engaged by individuals in overcontrolled typology, and functional coping was primarily engaged by resilient, emotionally stable showed a substantially mixed tendency about coping (and emotions as well). Nonetheless, they might be not at risk for depression, as demonstrated by our results that can be further understood by considering the personality dimensions adopted. The clusters identified, which can be interpreted in line with the literature about the personality typology (e.g., Asendorpf et al., 2001; Berry et al., 2007; Steca et al., 2010; Steca et al., 2007) was based on the Big Five model (Costa & McCrae, 1986). The clusters partially replicate the three typologies obtained but the further discriminant analysis also suggested an interpretation of the clusters on the basis of the two super-factors Stability (Neuroticism, Agreeableness, and Conscientiousness) and Plasticity (Extraversion and Openness) which have been confirmed by DeYoung (2006; DeYoung & Gray, 2009; DeYoung et al., 2002). In fact, the cluster identified can be also considered as characterized with different level of plasticity and stability. Resilient individuals resulted charcaterized with greater stablity and plasticity, emotionally stable with lower plasticity but greater stability, and overcontrolled individuals were characterized with lower stability and greater plasticity. Now, this

result is particularly interesting if compared to the hypothesis that stability accounts for the individuals differences on serotonergic system and plasticity on the dopaminergic system (cf. DeYoung, 2006; DeYoung & Gray, 2009). This may support our result that overcontrolled individuals (low on stability and high on plasticity) scored higher on depression; together with the heritability of personality traits and their linkage with depression, this provides support to hypothesize that these three clusters may differ on physiological mechanism that leads to depression. However, more investigation is needed as no phsyiological parameters were assessed in our study. What we essentially found is in line with previous studies that indicated resilient to show a substantial well-functioning, emotionally stable (referred to as undercontrolled) may show either functional and dysfunctional aspects, but yet they seemed not to be at risk for depression. Overcontrolled individuals resulted the more dysfunctional profile of personality along with emotional and coping strategies correlates. In sum, in line with the person-centered approach we enlightened emotional and coping strategies patterns that may ultimately be associated with mental health. These typologies are also very relevant in the context of health-care and chronic illness cure, since emotions, behavior, coping strategies and depression may contribute to determine patients' health (physical or mental). Furthermore, clinicians could adopt such typologies to predict, for instance, adherence to medications, or the adoption of dysfunctional coping, such as alcohol use, in order to prevent possible negative consequences.

4.4.6 Limitation and future direction

This study was conducted on a large sample of individuals recruited with snowballing sampling technique. For this reason, our results may be hardly generalized to the general population; moreover, the study was cross-sectional and there were no physiological measurements; thus, directionality or any physiological pathway may be hard to establish. However, we believe that these results may be of extreme interest for those who deal with individuals at greater risk for depression and in the contexts of health-care. In fact, these typologies may help clinicians to individuate patients that could be at greater risk for depression and eventually to discontinue the medication prescribed. In line with this hypothesis, we have gathered data on the specific population of HIV-positive which are at greater risk for depression, and we intend to apply the same clusters to this population. Furthermore, we have also follow-up after 8 months and then we will test these profiles' predictability on behaviors and physical as well as mental health.

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Table 1 Descriptive statistics of the three clusters formed

	Cluster 1	Cluster 2	Cluster 3
Percentage	39.1%	33.8%	27.1%
Sample size	373	323	259
		Cluster means	
Openness	4.04	3.21	3.39
Emotion Stability	3.08	3.21	2.12
Agreeableness	3.64	3.35	2.97
Energy	3.42	2.93	3.16
Conscientiousness	3.85	3.46	3.30

Table 2 Standardized coefficients (rotated, varimax) of the discriminant functions

	Functions	
	Plasticity	**Stability**
Openness	**.81***	-.03
Energy	**.39***	-.21
Emotion stability	-.19	**.87***
Agreeableness	.27	**.54***
Consciousness	.31	**.32***
Clusters' centroids of the two functions		
Overcontrolled	-.54 M	-1.73 L
Emotionally stable (Undercontrolled)	-1.11 L	.58 M
Resilient	1.34 H	.70 H

* $p < .01$

Table 3 Clusters' differences on emotions (ANOVA and Tukey post-hoc)

		Tukey post-hoc	
	F	**LOW**	**HIGH**
Joy	27,15 ***	1 (*M* = 3.19), 2 (*M* =3.36)	3 (*M* =3.62)
Interest	45,57 ***	1 (*M* = 3.29), 2 (*M* =3.17)	3 (*M* =3.82)
Attentive	44,81 ***	1 (*M* = 3.21), 2 (*M* =3.29)	3 (*M* =3.74)
Distress	47,82 ***	2 (*M* = 2.20), 3 (*M* =2.22)	1 (*M* =3.62)
Anger	148,42 ***	2 (*M* = 2.30), 3 (*M* =2.31)	1 (*M* =3.35)
Fearful	21,45 ***	2 (*M* = 1.73), 3 (*M* =1.68)	1 (*M* =2.08)

*M clusters' mean; *** p < .001; the numbers out of the parenthesis indicate the clusters: 1 "overcontrolled", 2 "emotionally stable", 3 "resilient"*

Table 4 EFA (PROMAX rotation) of the 14 items referred to coping strategies

	Factors				
	1	**2**	**3**	**4**	**5**
ITEM-1	**.79**	-.07	.03	.09	-.00
ITEM-4	**.46**	.19	.04	.01	02
ITEM-5	-.03	**.99**	-.03	-.02	.04
ITEM-2	.02	**.31**	.15	.13	-.18
ITEM-6	.05	-.03	**.71**	-.12	-.01
ITEM-11	.04	-.00	**.62**	-.09	.04
ITEM-7	-.29	.07	**.33**	.13	.01
ITEM-12	.14	.02	-.18	**.58**	.05
ITEM-8	-.08	-.03	-.08	**.49**	-.04
ITEM-10	.08	-.15	.28	**.34**	.05
ITEM-13	.03	.017	.02	.048	**.80**
ITEM-14	-.08	.07	.01	.09	**.53**

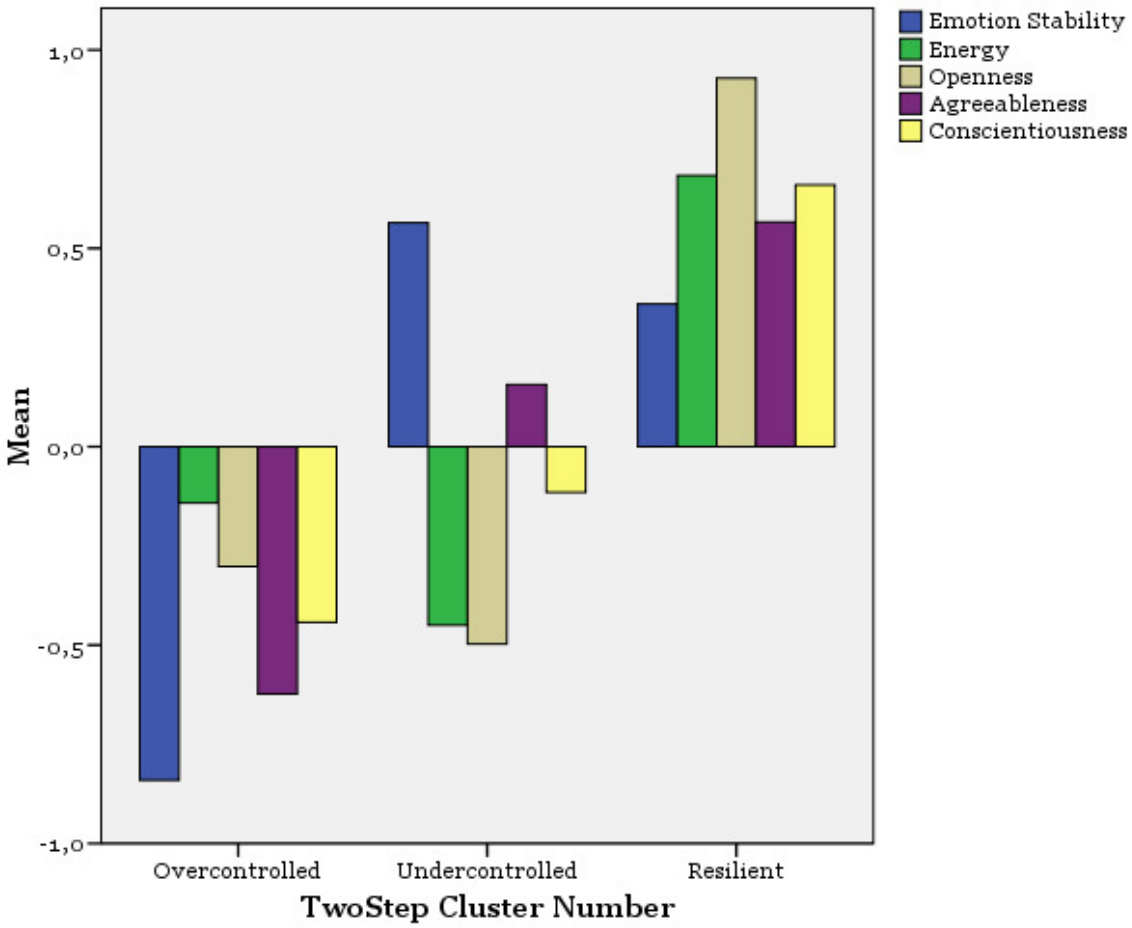
Note: Items refer to the items built to assess coping strategies

Table 5 Clusters' differences on coping strategies (ANOVA and Tukey post-hoc)

Coping	F	Low	Moderate	High
Avoidance	14,57***	3 (*M* = 3.67)		1 (*M* = 4.17), 2 (*M* = 4.08)
Passive	35,48***	3 (*M* = 5.89)	2 (6.28)	1 (*M* = 7.03)
Seeking social support	6,67***	1 (*M* = 5.28), 2 (*M* = 5.09)		2 (*M* = 5.09), 3 (*M* = 5.46)
Re-appraisal	6,80***	1 (*M* = 4.86)		2 (*M* = 5,15), 3 (*M* = 5.17)
Active	27,67***	1 (*M* = 5.90), 2 (*M* = 6.03)		3 (*M* = 6.47)
I drink alcohol to make myself feel better	10,16***	2 (*M* = 1.43), 3 (*M* = 1.40)		1 (*M* = 1.66)
I've been trying to find comfort in my religion	4,09*	1 (*M* = 1.53), 2 (*M* = 1.69)		2 (*M* = 1.69), 3 (*M* = 1.72)

** p < .05, *** p < .001; the numbers out of the parenthesis indicate the clusters: 1 "overcontrolled", 2 "emotionally stable", 3 "resilient"; the clusters that differed have been reported in separate rows; cluster within the same row did not differ significantly.*

Figure 5 Clusters' description respect to their mean score on the Big Five dimensions



Note: the label undercontrolled is used here to compare our results with the literature about typology, however, this cluster has been accordingly re-labeled "emotionally stable" on the basis of the discriminant analysis.

4.5 A Psychometric Investigation of Minority Stressors and Their Association with Perceived Stress among Gay and Bisexual Men

Norcini Pala, A, Dell'Amore, F., Steca, P.

Abstract

Minority stress is an additional load of stress that members of minority group experience because of the stigma manifestations that affect them. This may help explaining why members of sexual minority group, such as gay and bisexual men, are at greater risk for mental disorders. The sources of minority stressors are manifestations of social stigma such as e.g., antigay objective events, expectations of discrimination, sexual orientation concealment, and internalized homophobia. With the present work, we aimed at verifying whether these manifestations are associated to greater perceived stress. Additionally, since no specific Italian-language psychometric instruments have been developed to date, we also developed an instrument to cover the psychosocial stressors linked to the minority stress model. Participants (N = 451) were gay and bisexual Italian men recruited via Internet. Based on English-language instruments, 50 items were developed in Italian to capture the sources of minority stress. Whereas, perceived stress was assessed with the Perceived Stress Questionnaire. The eight factors extracted included antigay events, expectations of discrimination (from society and from family), sexual orientation concealment, internalized homophobia (towards the self and towards others), lack of rights for same-sex couples, and expectations of prejudice. The results of Structural Equation Model indicated that the stressors were significantly associated with each other. The exposure to antigay episodes, expectations of familial discrimination, and self-directed internalized homophobia were highly correlated with elevated levels of perceived stress. In conclusion, the instrument developed ad-hoc allowed us to confirm both the dimensionality of minority stress and that the manifestations of stigma that are more likely to increase perceived stress are those more proximal to the self.

Key words: Minority stress; Stress perception; Sexual orientation; Gay and bisexual men; Stigma; Heterosexism.

4.5.1 Introduction

Developing the minority stress model, Meyer (2003) has widely influenced the researches on minority groups' mental health, which have actually produced evidences about its importance (Grella, Cochran, Greenwell, & Mays, 2011; Hatzenbuehler, McLaughlin, Keyes, & Hasin, 2010; Meyer, 2007; Schwartz & Meyer, 2010). For instance, the model has been applied to explain the high rates of depression among gay and bisexual individuals as for instance depression (Hatzenbuehler, Nolen-Hoeksema, & Erickson, 2008; Mays, Cochran, & Roeder, 2003). Thus, minority stress model is currently considered a fundamental reference for psychosocial researchers and helped explaining the higher rates of mental disorders among gay and bisexual individuals respect to their heterosexual counterparts.

The model consists in minority stressors that are thought to produce the so-called minority stress, which is a very specific form of social stress essentially generated by the conflict between members of minority groups and the society they live in (Lazarus & Folkman, 1984; Pearlin, 1999). Indeed, assuming that a harmonious relationships are the basis for a healthy living (Selye, 1982), when conflicts occur individuals may, then, experience greater stress (Meyer, 2003). In fact, this might be the case of members of minority groups that for their disadvantageous social position and unfavorable condition they have to live in. Additionally, they also deal with the stigma

manifestations (minority stressors) that, then, produce minority stressors (Meyer, 1995, 2003). However, it should be noted that, although stress researches may provide information on the connection between stressors (the source), stress (the response), and illness (the consequence), the measures adopted may sometimes ingenerate confusion (Dohrenwend et al., 1984; Lazarus, DeLongis, Folkman, & Gruen, 1985). This may be the case of studies about the sources of minority stress and mental illness, which have actually found significant and recurrent associations (e.g. Grella, Cochran, Greenwell, & Mays, 2011; Hatzenbuehler, McLaughlin, Keyes, & Hasin, 2010; Hatzenbuehler, Nolen-Hoeksema, & Erickson, 2008; King et al., 2008; Mays, Cochran, & Roeder, 2003; Meyer, 1995, 2003, 2007; Schwartz & Meyer, 2010). Although it is known that minority stressors are effectively associated with mental illness, is not clear if this is due to the greater stress generated. Thus, we conducted this study, in order to verify whether minority stressors were associated with greater perceived stress.

4.5.2 Minority stressors: The manifestations of social stigma

In order to clarify the concept underlying the minority stress model, the main axioms described by Meyer (1995, 2003) should be briefly discussed. Namely, minority stress is a chronic form of stress because it is caused by stable social and cultural processes. Additionally, it is, of course, socially based as social processes, institutions, and structures generate it. Lastly, minority stress is "unique" because members of minority groups (stigmatized) experience minority stress in addition to "general stress", which is in fact also experienced by members of non-stigmatized groups. Thus, minority stress represents an additional load of stress for members of minority

groups and this is might help explaining the reason why they are more vulnerable to mental illness (Meyer, 1995, 2003).

The sources of minority stress are deeply rooted into the social processes, dynamics and structures, and are the products of the social stigma that affects members of minority groups. As mentioned before, minority stressors are indeed manifestations of the stigma, four of which were described by Meyer and, in a second time, by Herek (2004, 2009, 2011) that added the macro-social, or structural, ones. The minority stressors might be placed on an ideal continuum from distal to proximal to the self (Meyer, 1995, 2003). The more distal one is "objective antigay events", namely the physical or verbal manifestations of stigma basically consisting in homophobic hate crimes towards gay and bisexual individuals. These antigay events are also very common within Italian schools with evident negative consequences on individuals' well-being (Prati, Pietrantoni, & Norcini Pala, 2009).

Moving on the continuum towards a more proximal stressor, Meyer (1995) placed the expectations of discrimination, namely the expectations to be treated unfairly and/or unequally respect to members of non-stigmatized groups. Such expectations may be reinforced by social and legal reactions to homophobic hate crimes that are not penalized by the law or condemned by the society and consequently homophobia might be perceived as "legalized" (Meyer, 1995). Additionally, this increases the perception of lack of safety for gay and bisexual individuals because of hostility of one's social environment (Herek, 2004, 2009). Moreover, individuals who have been victimized for their sexual orientation could also expect future discriminations to occur (Kelleher, 2009), and then may feel the need to keep high level of vigilance, which actually might produce minority stress (Meyer, 1995).

The expectations of discrimination are also reinforced by the social and legal rights disparities and by the lack in anti-discrimination laws as well (Herek, 2009) a social scenario very common in predominantly Catholic European countries such as Italy where indeed there is scarce support for gay and bisexual individuals (Gerhards et al., 2010). This, of course, also contributes in generating the perception of social hostility towards gay and bisexual individuals. In line with Herek (2011), indeed, the lack of legal rights for same-sex couples and/or the lack of clear legislation against discrimination or homophobic aggressions could promote the perception of social disparities. Therefore, based on these premises, Italy, respect to northern European countries, which are predominantly protestant (Gerhards et al., 2010) could be perceived essentially a homophobic society. Therefore, Italian gay and bisexual individuals are very likely to conflict with the "dominant" heterosexist society. In addition, the legal issue of discriminations is very controversial since the discriminations based on one's sexual orientation are legally sanctioned, as sexual orientation is considered a personal and social condition. However, "one of the main deficiencies of the civil law regulation is that it only provides protection if the speech is targeted directly at identifiable individual(s), which makes the regulation difficult to use against general homophobic expressions, no matter how harmful they may be" (Gasparini, La Torre, Gorini, & Russo, 2012; p. 208). Thus, gay and bisexual individuals may experience greater stress for the efforts required to adapt to the unfavorable legal and social conditions they have to live in (Herek, 2011). Meyer (1993, 2003) also described a third source of minority stress, the sexual orientation concealment that may be adopted as a self-protective strategy in order to reduce the risk of discrimination or the hate crime (Meyer, 1995, 2003; Pietrantoni et al., 2008). However, sexual orientation concealment requires great efforts that may turn into greater (minority) stress. Lastly, social stigma may be interiorized by gay and

bisexual individuals, showing then negative attitudes towards homosexuality and homosexuals persons, as well as towards self (Herek, 2004; Meyer, 2003). This may be the consequence of growing up within a homophobic environment (e.g. family and society) and, later on, when individuals realize their sexual orientation, they direct the negative attitudes towards themselves. Internalized homophobia, obviously, generates great psychological distress due to the resulting psychological conflicts and since it is strictly related to the self, as indeed Meyer (2003) pointed out defining it as the most insidious and proximal source of minority stress (Meyer & Dean, 1998).

More recently, Herek (2011) described another stressor that defined macro-social or structural, consisting in those social processes that convey societal stigma towards gay and bisexual individuals, producing then minority stress. For instance, the absence of legal rights for same-sex couples could reinforce the perception of societal heterosexism. Social and legal right may be considered objective, however, in this work we assess individuals' perception of such stressor. In other words, we are investigating the impact of the appraisal of such a stressor, which is linked to stigma and conveys society's homophobic attitudes (Herek, 2011). Lastly, we also investigated another aspect of social stigma that is the stereotypical contents of antigay prejudice (Herek, 1991). In line with minority stress model, we assessed one's expectations of being stereotypically defined as being pedophilic, perverted and abnormal (see Boysen, Vogel, Madon, & Wester, 2006; King, 2004; Simmons, 1965).

4.5.3 Gay and bisexual men differences on minority stressors

From the literature about the minority stressors clearly emerged another relevant aspect that should be investigated, namely the role of sexual orientation. Previous studies, indeed, suggested that gay and bisexual men are more likely to experience

minority stressors than lesbian and bisexual women are (Cochran, Keenan, Schober, & Mays, 2000; Cochran, Sullivan, & Mays, 2003; King et al., 2008; Mays & Cochran, 2001). Gay and bisexual men are greater risk of being victims of antigay hate crimes compared with lesbian and bisexual women. This may be a consequence of their greater visibility and/or because male homosexuality is less accepted than female homosexuality (Herek, 2009; Prati, Pietrantoni, & Norcini Pala, 2009). Moreover, bisexual men tend to conceal their sexual orientation; therefore, although gay men might be more visible than bisexual men and are at greater risk of being victims of homophobic activities, bisexual men have been shown to have greater levels of internalized homophobia than gay men (Stokes, Vanable, & McKirnan, 1997). Therefore, the present study will focus on gay and bisexual men.

The sources of minority stress may be highly correlated as they could co-occur or co-exist. Therefore, i.e., the victims of antigay hate crimes might expect to be victimized or discriminated against in the future, and might show great discomfort with their sexual orientation (Meyer, 1995, 2003; Meyer & Dean, 1998; Miller & Major, 2000; Ross et al., 2010). Consequently, they could decide to conceal their sexual orientations (Kelleher, 2009; Meyer, 2003, 2007). For this reason, we also aimed at testing a model in which the stressors described above correlate and are associated with perceived stress.

4.5.4 Aims

With the present work, we aimed at exploring the dimensionality of minority stress model, in order to define, psychometrically, the sources of minority stress that gay and bisexual men in Italy may experience. This would also allow us to test their correlation and association with perceived stress, a subjective assessment of stress

reaction, which results to be the more influential aspect of stress (Lazarus, 1966, 1977). To the best of our knowledge, the instruments developed for assessing minority stressors were mainly in English-language and not available in Italian-language. For this reason, therefore, we built an instrument inspired on such questionnaires rather than translating them. Our intent was to developed an instrument conceptually based on validated instruments but able to capture the specific characteristics of the Italian society. Additionally, the procedure of translation is extremely important, as it must overlap exactly the intentions of the authors of the original instrument. Thus, translation may lead to a loss of subtle meanings and shades, and semantic contents, resulting then far too difficult and ultimately misleading. Nonetheless, there are substantial differences between Italian and American society, also related to laws; therefore, we opted for developing an ad-hoc instrument for the topic investigated in this study might be sensitively influenced by the culture and society.

To pursue our goals we built items to cover the stigma manifestations discussed within the introduction, namely (1) objective antigay events, (2) expectations of discrimination, (3) internalized homophobia toward others, (4) internalized homophobia toward the self, (5) sexual orientation concealment, (6) expectations of prejudice, and (7) lack of rights for same-sex couples. Based on Meyer's (1995, 2003) and Kelleher's (2009) studies we also tested whether having experienced antigay episodes was associated with having greater expectations of discrimination and higher levels of discomfort with one's own sexual orientation (internalized homophobia towards self). Additionally, it has been tested whether the lack of rights for same-sex couples and the expectation of prejudice were associated with an increased expectation of being discriminated against in the future because both the

lack of rights and the expectation of prejudice were considered to be structural stressors that were derived from social processes (see Herek, 2011). Possible associations between concealing one's sexual orientation and expectations of discrimination and greater degrees of internalized homophobia were also evaluated. It was predicted that participants who had higher levels of expectations of discrimination and internalized homophobia would be more likely to conceal their sexual orientation than participants who had lower levels of these two factors (Figure 1; see Meyer, 1995, 2003). Lastly, the association of participants' sexual orientation with the sources of minority stress was evaluated, expecting to find bisexual men with higher levels of expectations of discrimination, greater sexual orientation concealment, and internalized homophobia respect to gay men (see Herek, 2009; Prati, Pietrantoni, & Norcini Pala, 2009; Stokes, Vanable, & McKirnan, 1997). The entire theoretical model is graphically represented on the Figure 1.

4.1.9 Methods

4.1.9.1 Participants and procedure

Participants (N = 451) were Italian men from Northern Italy (55.7%), Central Italy (29.3%), Southern Italy (10.2%) and the Italian Isles (4.4%). They ranged in age from 18 to 68 years, and their mean age was 31.92 (SD ± 9.75) years. The sample was composed of gay (93.1%), bisexual (6%), and heterosexual men (n = 2, 0.4%; missing data 0.4%). Heterosexual men were excluded from the analysis to avoid misleading results. Less than one percent of the participants had only completed an elementary education (0.2%), 4.3% of the participants had completed junior high school, 42% of them had high school diplomas, 18.7% of the participants had university degrees, 24.9% of the participants had master's degrees, and 9.9% of the participants had

Ph.D. degrees or other specializations. Recruitment for participation in the present study took place during April 2010 over a 4-day period, and it was accomplished via www.gay.it, which is one of the most popular Internet sites used by gay and/or bisexual men in Italy. Because this study was Internet-based, the procedure for obtaining informed consent was structured as follows: a general recruitment message that contained the subject of the survey along with the names and affiliations of the authors was posted on the www.gay.it website. The recruitment message also contained a link to the homepage of the survey, and further information about the study was provided on its homepage. Specifically, the voluntary nature of participation in the study and the anonymity of the participants' data were constantly stressed. Participants were not asked to provide any personal information, and they were provided with an email address for the first author that they could use to request further information. Finally, the homepage of the survey site contained two separate links, which participants could use to declare either "I am under 18 years of age" or "I am over 18 years old, and I want to participate in the survey". Participants who clicked on the first link, thereby declaring that they were under the age of 18 years, were then redirected to a page on which the exclusion criteria for the study were reported. Participants who clicked on the second link, thereby declaring that they were over the age of 18 and that they wanted to participate in the survey, completed the questionnaires and submitted them to the first author's e-mail address. This procedure allowed the survey to be conducted in a completely anonymous manner. Participants declared themselves to be over 18 years of age. Individuals who were under the age of 18 years were excluded from the analysis because parental permission for their participation would have been required. This study was conducted in accordance with the Code of Ethics of the World Medical Association (the Declaration of Helsinki).

4.5.5 Measures

Minority Stressors. In accordance with the definitions of minority stressors provided by Meyer (1995, 2003) and Herek (2004, 2009, 2011) an Italian-language psychometric instrument was developed. Fifty items built for covering seven theoretical dimensions that are listed and numbered (in the parentheses) below. Additionally together with a brief introduction of the dimensions, we also reported examples items (of English-language validated instruments) on which we based the Italian-language items developed.

(1) For the assessment of "antigay objective events", were built items inspired on the following meaningful items "Have you been assaulted because of being gay?", "Have you been harassed or discriminated against professionally because you were gay?" and "How many times have you been rejected by family members because you are a gay/bisexual man?" (Hamilton & Mahalik, 2009; Hatzenbuehler et al., 2008; Kimmel & Mahalik, 2005; Meyer, 1995; Szymanski, 2006; Zamboni & Crawford, 2007). For these items we chosen a 5-point scale assessing the frequency with which participants experienced episodes of physical and verbal aggression, discrimination and social exclusion. Thus, they were asked to rate items from 1 (Never) to 5 (Always).

(2) The expectations of discrimination were assessed through items built reflecting the contents of the following example items: "I believe the world is a dangerous place for gay people," "Once they know a person is gay, most people will take his opinion less seriously," and "In the last 12 months, I have perceived a rise in homophobia" (Hatzenbuehler et al., 2008; Martin & Dean, 1987). The expectations of discrimination items could be worded to reflect either a general or specific social context (e.g., within the participant's family or at his workplace). We hypothesize the context to be particularly important for these items since the contexts in which

discrimination occurs may differently influence individuals' perception of stress (e.g., "Most people would willingly accept a gay man as a close friend," vs. "Most employers will pass over the application of a gay man in favor of another applicant"). Therefore, items were generated generally and specifically worded referred to the expectations of discrimination from family members, friends, doctors and healthcare providers, as well as within the workplace environment. Items were rated on a 5-point likert type anchored to agreement labels: from 1 (Completely disagree) to 5 (Completely agree).

(3) Sexual orientation concealment was assessed by developing items based on the following significant example items: "It is important for me to 'be out' to straight people I know," and "Are you worried, concerned, or afraid that people will find out that you are lesbian/bisexual/gay?" (Mohr & Fassinger, 2000). We aimed at capturing respondents' beliefs about coming-out (e.g., their fears of rejection and/or isolation); items were rated on a 5-point scale in which a score of 1 expressed disagreement (Completely disagree) and a score of 5 expressed agreement (Completely agree). In addition, the extents of individuals "coming-out" was assessed by asking whether they had come out to their parents, as well as asking with whom they shared their romantic experiences (parents, siblings, friends, and relatives). In this case, items were rated with a 2-point answer scale 1 (Yes) and 2 (No).

Internalized homophobia was operationalized as directed toward self (4) and towards the others (5), in line with Herek's (2004) definition. The items built were related to the following examples: "If someone offered me the chance to be completely heterosexual, I would accept the chance," "I hate myself for being attracted to other men/women," "I live in fear that someone will find out I am a gay or lesbian/bisexual man/woman," and "How comfortable do you feel about being gay?" (Hatzenbuehler et al., 2008; Herek et al., 2000; Kashubeck-West & Szymanski, 2008; Martin &

Dean, 1987). In addition, based on the Revised Nungesser Homosexuality Attitudes Inventory (RNHAI; Mayfield, 2001; Shidlo, 1994), which assesses both sub-dimensions of internalized homophobia, we also built items conceptually based on the following examples "I wouldn't mind if my boss knew that I was gay," and "There have been times when I've felt so rotten about being gay that I wanted to be dead." The items for both dimensions were rated on a 5-point Likert scale that ranged from 1 (Completely disagree) to 5 (Completely agree).

(6) The lack of rights for same-sex couples is of course an objective social issue, in Italy, indeed, still there are not nor legal or social rights. For our study, we focused on individuals' perception of such a lack concretely operationalized as the perception of social barriers for same-sex couples. The examples of items, on which we built the items are "How important is having the availability of legalized same-sex marriage to you?" and in general the works of Herek (2009, 2011). Participants rated their agreement a 5-point scales that ranged from 1 (Completely disagree) to 5 (Completely agree).

Lastly we also included items on (7) the expectations of prejudice that were meant to capture individuals' expectations about being stereotypically labeled as a perverted, abnormal, and/or pedophilic person (see Bernstein, 2004; Herek, 1991, 2002; Simmons, 1965). Participants rated these items on a 5-point scale anchored to agreement labels ranged from 1 (Completely disagree) to 5 (Completely agree).

Perceived stress was assessed through the Italian version of the Recent Perceived Stress Questionnaire (Levenstein et al., 1993). This instrument allowed evaluating the level of stress experienced by the participants that rated the items on a 4-point scale with frequency labels ranging from 1 (Almost never) to 4 (Usually).

In this paper, the brief version proposed by Fliege et al. (2005) was used, as it resulted with a more reliable factorial structure respect to the original version. The brief version was composed of 4 factors underlying a second order factor labeled as "perceived stress". The first order factors assessed worry (5 items; e.g. "You have many worries," "You fear you may not manage to attain your goals,"); tension (5 items; e.g. "You feel tense," "You feel mentally exhausted"); lack of joy (5 items; "You feel you're doing things you really like," "You are full of energy," the items were all positively worded thus they were inverted for the analsys); demands (5 items; "You have too many things to do," "You feel that too many demands are being made on you"). Thus, the perceived stress assessed through this instrument was generally referred to the stress manifestations.

4.5.6 Data Analyses

Statistical analyses were conducted using SPSS 15.0 (Statistical Package for the Social Sciences; Chicago, IL) and Mplus 6.11 (Muthén & Muthén, 2010). Both the skewness and kurtosis of the distributions of the variables were assessed; skewness or kurtosis values of less than |1| indicated the normal distributions of the data, whereas values that were greater than |1| indicated that the variables were non-normally distributed. Several variables violated the normality assumption, and therefore, they were treated as ordinal variables.

Exploratory Factor Analyses (EFAs) and Structural Equation Modeling (SEM) were performed using Mplus 6.11. The Weighted Least Squares Method (WLSM) was used for these analyses because they included a variety of variable types (ordinal, continuous, and binary variables) (Brown, 2006; Finney & DiStefano, 2006; Flora & Curran, 2004; Muthén & Muthén, 2010).

The number of factors that were to be extracted for a given model (EFA - Promax rotation) was determined by considering three criteria: having an RMSEA of < .06 (Steiger & Lind, 1980), the scree plot, and the factor interpretability.

Goodness-of-fit indexes for SEM included the Tucker-Lewis Incremental fit index (TLI; Tucker & Lewis, 1973), the Comparative Fit Index (CFI; Bentler, 1990), the RMSEA and the χ^2/df ratio (Crowley & Fan, 1997). CFI and TLI scores that were ≥ .95 indicated that the model had a good fit, and scores that were ≥ .90 indicated that it had an adequate fit. RMSEA scores that were less than or equal to .05 indicated that the model had a good fit, and an RMSEA score that was or equal to .08 indicated an adequate model fit. A χ^2/df ratio of less than 5 indicated that the model had a high level of fitness (Bollen 1989; Crowley & Fan, 1997; Hu & Bentler, 1999; Muthén & Muthén, 2004; Schermelleh-Engel, Moosbrugger, & Müller, 2003; Yu & Muthén, 2002).

4.5.7 Results

4.5.7.1 Minority Stress Questionnaire - Exploratory Factor Analysis (EFA)

Two EFAs were performed; the second EFA excluded variables for which the results of the first EFA had shown factor cross-loadings that were greater than .30 or loadings that were less than .30 (e.g., Item 24 "The Italian State does not confer all civil rights upon me," Item 26 "Gay and bisexual men are easily identifiable," Item 27 "I avoid physical contact with men because it feels uncomfortable," Item 39 "I like to act in an effeminate manner," Item 41 "I try to act masculine," Item 42 "I freely speak of my sexual orientation with my colleagues," Item 49 "Coming-out to my friends is not important to me"). The cutoff loading magnitude of .30 was selected in accordance with Nunnally's (1978) guidelines, which have been widely accepted. A

total of 8 factors that had eigenvalues that were greater than 1 were extracted (RMSEA = .044; see table 1). An analysis of the content of the included items confirmed the adequacy of factor interpretability, and the Cronbach's alphas that were obtained for these factors indicated good factor reliability. There was a partial overlap between the 8 factors that were extracted and the 7 factors of our theoretical model. The extra factor that was extracted referred to the respondents' expectations of being discriminated against by their family members. This is notable because antigay events items about objective events of discrimination were included (e.g., "I have been discriminated against"). However, those items tended to be loaded on expectations of discrimination from society. Thus, it is likely that events of discrimination are more subtle than the explicit physical or verbal antigay aggressions, and they are therefore perceived more subjectively as being acts of aggression. Each of the extracted factors is described below, and the descriptions include the number of items for each factor, the Cronbach's alpha and item examples.

Antigay objective events (3 items, α =.754). This dimension reflected the frequency of antigay events that the participants had experienced in the past (e.g., "I have been verbally attacked," "I have been physically attacked," and "I have been discriminated against").

Expectations of discrimination from society (12 items, α = .852). This factor represented the expectations of discrimination that the participants experienced. The content of the included items referred to both general expectations of discrimination (e.g., "I expect to be insulted or verbally harassed") and expectations of discrimination from colleagues, friends, and medical professionals (e.g., "I expect to be discriminated against by the doctor").

Expectations of prejudice (3 items, α = .922). This dimension reflected individual expectations regarding being the target of a prejudicial stereotype (e.g., “As a homosexual/bisexual, I could be considered: ‘abnormal’, ’perverted’, ‘a pedophile’”).

Internalized homophobia toward others (6 items, α = .751). This dimension reflected the negative attitudes toward homosexuality and homosexual persons that were held by the participants, therefore indicative of homophobia toward others (e.g., “I feel very uncomfortable when I see an effeminate man” “If I see two men kissing in the street, I feel: (i) Extreme discomfort; (ii) Strong disgust”).

Expectations of discrimination from family (3 items, α = .859). This dimension referred to individual expectations of discrimination within the family environment (e.g., “I don’t think my family would accept me,” and “As a homosexual/bisexual, I am afraid of being discriminated against by my family members”).

Internalized homophobia toward the self (6 items, α = .915). This dimension assessed the homophobic attitudes that the individuals directed toward themselves (e.g., “I avoid any physical contact with people of my sex because I find it embarrassing,” “I wish I weren’t homosexual/bisexual,” and “My sexual orientation makes me feel really bad”).

Lack of rights for same-sex couples (3 items, α = .751). This dimension assessed a macro-social stressor, namely the societal heterosexism that results in the limiting of rights for same-sex couples (Herek, 2011; e.g., “I will never be able to marry,” “I will never be able to adopt children,” and “I will never be able to legalize my relationship”).

Concealment of sexual orientation (7 items, α = .840). This dimension reflected the extent to which an individual had come out and the individuals’ beliefs that were

related to coming-out (e.g., “My father knows I am gay/bisexual,” “My mother knows I am gay/bisexual,” and “Nobody knows I am gay/bisexual”).

4.5.8 The Association of the Sources of Minority Stressors with Perceived Stress

A Structural Equation Model was performed in order to test the reciprocal associations of minority stressors and to test their associations with perceived stress. Results, reported in figure 2, were slightly different from our expectations previously discussed ad graphically illustrated within the theoretical model. Results were graphically represented and in order to improve model readability, non-significant associations ($p > .05$) have been excluded. The ellipses in Figure 2 represent latent variables; their indicators were excluded to improve the readability of the figure. Sexual orientation was a self-reported “observed variable” and therefore presented in a square, it was coded as follows 1 – bisexual men and 2 – gay men.

The goodness of fit of the model was acceptable ($\chi^2/df = 3.37$, CFI/TLI .919/.910, RMSEA = .070). The loadings of the antigay objective events items ranged from .617 to .779; the loadings of the expectations of discrimination from society items ranged from .499 to .771; the loadings of the expectations of prejudice expectations items ranged from .673 to .903; the loadings of the internalized homophobia toward others items ranged from .828 to.921; the loadings of the expectation of discrimination from family items ranged from .530 to .926; the loadings of the sexual orientation concealment items ranged from .454 to .937; the loadings of the internalized homophobia toward the self items ranged from .622 to .951; and the loadings of the lack of rights for same-sex couples items ranged from .870 to .920. The loadings of the PSQ items on the first-order factors ranged from .320 to .782. The second-order latent variable labeled “perceived stress” showed loadings ranging from .785 to .940.

The perception of the lack of same sex couples rights (structural stressor) was associated with prejudice expectations and expectations of discrimination from family and friends; whereas, prejudice expectations correlated just with the expectations of discrimination from society. The factor "antigay objective events" was associated with both expectations discrimination from family and friends, and expectations of discrimination from society, as well as with perceived stress. Expectations of discrimination from society, together with expectations of discrimination from family and friends, were reciprocally correlated and were associated with internalized homophobia towards the self. Expectations of discrimination from family and friends, instead, correlated also with internalized homophobia towards the others. These expectations, along with internalized homophobia towards the self, were both correlated with sexual orientation concealment and greater perceived stress. Lastly, individuals' sexual orientation was significantly associated with expectations of discrimination from family and friend and with internalized homophobia towards others. Sexual orientation was coded as follow bisexual men (1) gay men (2), thus, results indicated that bisexual men were more likely to expect to be discriminated by family and friends, and show greater internalized homophobia towards the others. No significant indirect effects on perceived stress were observed.

4.5.9 Discussion

Meyer's (1995, 2003) minority stress model has substantially modified scientific community approach to minority groups' health and offered a valid framework to explain the greater rates of mental disorders (e.g. depression) among gay and bisexual individuals (see also Grella et al., 2011; Hatzenbuehler et al., 2010;

Hatzenbuehler et al., 2008; King et al., 2008; Mays, Cochran, & Roeder, 2003; Meyer, 2007; Schwartz & Meyer, 2010). The central role of social stigma and more precisely its manifestations, considered as the sources of minority stress is largely discussed within the model. Based on minority stress model, then, gay and bisexual men, but more generally all members of minority groups, might experience greater load of stress than non-stigmatized individuals might. This additional load of stress might be, then, the cause for the greater incidence of mental disorders among gay and bisexual men. Minority stressors are strictly and deeply embedded into societal processes and structures and the results of the studies conducted so far, mainly in English cultures, may be not extendable to non-English cultures. On the other hand, more plausibly, may need major adjustments. Therefore, we conducted this study to investigate the sources of minority stress exploring the dimensionality of minority stress model anchoring our work to the results of international studies. Indeed, to date, to the best of our knowledge, no studies were conducted so far in order to investigate minority stress model in Italy neither psychometric instruments for the minority stressors assessment were available in Italian-language. Therefore, we preceded formulating items conceptually based on the English-language instruments but adapted, into their wordiness, to the social and legal conditions that Italian gay and bisexual individuals experience. Additionally, differently from the major of the validated instruments, we also evaluated the role of the different life domains in which minority stressors may occur. Although the instrument built for this study may need further revision, and investigation, in order to assess its psychometric properties and reliability, it may offer preliminary insights on the sources of minority stress in a non-English country.

Minority stress was theorized as an adjunctive portion to general stress that gay and bisexual men may experience due to the stigma manifestations (Meyer, 1995, 2003). The present work may support this assumption by confirming the dimensionality hypothesized by Meyer (1995, 2003) and Herek (2004, 2009, 2011). Thus, the psychometric evaluation of the dimensionality of the model leaded us to individuate eight minority stressors. Namely, objective antigay events, expectations of discrimination from society, and from one's family internalized homophobia toward the self, and the others, sexual orientation concealment, the lack of pro-same-sex rights legislation, and the expectations of prejudice. The expectations of discrimination showed up as composed of two main domains: general expectations (coming from society) and contextualized expectations (coming from one's family). This result supports our hypothesis that the context in which the manifestations of stigma occur may be significant. However, we also underline that this result could reflect the importance given to family in Italian culture. This result should encourage further investigation in order to highlight cross-cultural differences.

Together with the expectations of discrimination, expectations of prejudice were also observed consisting in individuals' expectations to be stereotypically judged as pedophiles, perverted, or considered abnormal because of their sexual orientations. Indeed, the social process of "labeling" leads to associate negative attributes to members of the labeled group (stereotype) and this, in its turn, might lead to greater discriminations (Link & Phelan, 2001). This is indeed is supported by our results, since the expectations of being stereotypically judged is associated with greater expectation of discrimination, basically for the stigma generated by the social labeling.

In line with Herek (2011), perceived structural stressor related to legislative barrier to the rights of same-sex couples was individuated. As hypothesized by the author, this stressor may promote the expectations of discrimination for the heterosexism overtly conveyed ad reinforced. The stigma manifestations identified in this work result associated, and we also hypothesize that stigma manifestations could exert different influence from distal to proximal, partially in line with Meyer (1995, 2003). Namely, objective antigay episodes increases the expectations of discrimination (e.g., by friends, in the workplace, by doctors and healthcare providers and by family members; see Meyer, 1995, 2003). Differently from our expectations, the victims of antigay hate crimes do not show greater internalized homophobia. On the other hand, in line with our hypothesis, expectations of discrimination, instead, may lead to greater internalized homophobia toward the self. Interestingly, only individuals who expect to be discriminated by their family show internalized homophobia toward others (Meyer, 1995, 2003). This might be interpreted as the confirmation that individuals who "learn" homophobic attitudes within their family environments initially direct homophobic attitudes toward others before directing them toward themselves (Herek, 2004). Additionally, we also hypothesize that the expectations of discriminations from one's family might be more invalidating, for the proximity to the self of the familial environment, and influent than the expectations of discrimination from the society. Sexual orientation concealment is consistently enacted by those who expect to be discriminated from family members and who suffer from internalized homophobia toward the self. This result may confirm that concealment could be viewed as a self-protecting strategy, namely individuals try to protect themselves by being target of antigay crimes. In fact, it might make feel members of minority groups to be perceived as non-target of stigmatization in line

with the assumption that some gay and bisexual men feel the need to be considered members of the majority group (see Chrobot-Mason, Button, & DiClementi, 2001).

The perceived structural manifestation of stigma is not associated with greater perceived stress but still it may generate expectations of prejudice and discrimination. In fact, the perception of the lack of rights for same-sex couples may be perceived as a social barrier that could essentially "legalize" homophobia. If society fails to provide laws against homophobic crimes and laws that protect the rights of same sex-couples, it thereby fails to support gay and bisexual men and women by and might thus be perceived as being hostile and unsafe (Herek, 2011). Lastly, individuals' sexual orientation might play a role on minority stressors; indeed, bisexual men result more homophobic towards homosexual individuals than gay men are. Additionally, they also show greater expectations of discrimination from their families. However, unlike what was expected, based on the current literature, no further association between perceived stress and sexual orientation was found.

Of the sources of minority stress tested, three of them are significantly associated with greater perceived stress namely, antigay objective events, expectations of discrimination from one's family, and internalized homophobia directed towards the self. Adopting the continuum hypothesized by Meyer (1995, 2003), these stressors can be described in terms of their locations on such a continuum referred to their proximity to the self. The distal and objective stressor (antigay hate crimes experienced) is located at one extreme of the continuum, the proximal, subjective stressor (internalized homophobia) is located at the other extreme, and the expectations of familial discrimination stressor might be placed in the middle. The impact on perceived stress results greater when comes from the most proximal (internalized homophobia towards the self). Then individuals who have experienced

negative events and who have no means of discussing these events with their families or receiving support from them may also experience greater stress (Lewis, Derlega, Clarke, & Kuang, 2006; Rosario, Schrimshaw, & Hunter, 2005; Ueno, 2005; Yoshikawa, Wilson, Chae, & Cheng, 2004). Therefore, having an unsupportive, homophobic family of course increases the likelihood that an individual will internalize homophobia (Meyer, 1995, 2003). Lastly, our result might be explained coherently with Gruenewald, Kemeny, Aziz and Fahey (2004), who claimed that the presence of stressors that threaten an individual's social identity may generate a more severe stress reaction (see also Dickerson, Gruenewald, & Kemeny, 2004; Dickerson, Mycek, & Zaldivar, 2008). Thus, we hypothesize that when one's identity is "at risk," perceived stress may be increased.

Taken together, then, our results suggest that certain stigma manifestations may increase perceived stress. Namely, objective antigay events, expectations of discrimination from one's family, and internalized homophobia directed towards the self are all likely to produce the so-called minority stress. The other stigma manifestations are rather reciprocally associated but were not found associated to greater perceived stress. Therefore, it is possible that the stressors associated with greater perceived stress could enhance the risk of mental disorders for the additional (minority) stress produced by stigma manifestations (Herek & Garnets, 2007; Meyer, 1995, 2003). However, we cannot exclude the others stigma manifestations to be influential on individuals' well-being, likely through a different path.

4.5.10 Limitation and future studies

Although the cross-sectional nature of the present study and the convenience sampling method used pose some limitations to the generalization of the results, our

findings might offer some useful insights regarding the concept of minority stress among gay and bisexual men. The fact that only gay and bisexual men were recruited might be a limitation of our study, and we have recently tried to overcome this limitation by evaluating the validity of the questionnaire in a sample of gay, lesbian and bisexual men and women. However, we encourage other researchers to use our instrument, which is freely available in both Italian and English language, and can be requested by contacting the first author of this paper. Additionally, we are interested in examining the cultural differences related to minority stress, for this reason the English version of the instrument could be used for this purpose. In fact, as minority stressors are substantially social stigma manifestations, culturally different societies might show different patterns as well as specific stressors.

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Table 1. EFA: Minority Stress Questionnaire item loading (8-factor model, RMSEA .044)

	1	2	3	4	5	6	7	8
MS-1	**.862**	-.003	.034	-.027	.038	.016	.011	.012
MS-2	**.686**	.123	-.093	.099	-.041	-.040	.109	-.031
MS-3	**.648**	.219	.016	-.068	.087	.009	-.041	-.019
MS-4	.182	**.546**	.054	.002	.024	.019	-.020	.016
MS-5	.022	**.617**	.043	-.077	-.072	-.082	-.049	.029
MS-6	.003	**.566**	.198	-.081	-.002	-.001	-.110	-.077
MS-7	-.005	**.635**	.078	-.081	-.109	.151	.004	-.014
MS-8	.064	**.498**	.160	-.058	.132	.064	-.064	.014
MS-13	.111	**.326**	.005	.127	.285	.054	.036	.240
MS-14	.058	**.640**	.055	-.052	-.064	.198	-.010	-.031
MS-15	-.069	**.566**	-.026	.109	.072	.029	.019	.157
MS-16	.036	**.572**	.020	.007	.213	-.040	.083	-.246
MS-17	-.009	**.538**	-.057	.021	.284	-.035	.015	-.222
MS-18	-.015	**.655**	-.012	.035	.082	-.038	.012	.113
MS-19	.084	**.427**	-.002	.205	.282	.034	.028	.128
MS-9	.007	.093	**.820**	.043	-.031	.052	-.048	.004
MS-10	.012	-.021	**.925**	.081	.002	-.009	.071	.045
MS-11	-.034	.019	**.817**	-.048	.021	-.045	.067	-.069
MS-30	-.052	.002	.006	**.869**	-.003	.073	.040	-.075
MS-31	.181	-.219	.078	**.868**	.218	-.009	-.128	.008
MS-32	-.064	.015	-.062	**.979**	-.086	.015	.065	-.084
MS-33	.041	-.117	.020	**.862**	.018	-.003	-.030	.051
MS-34	-.162	.161	.022	**.388**	.031	.260	.013	.038
MS-25	-.217	-.007	-.031	**.509**	.054	.191	-.054	.000
MS-12	-.041	.023	.043	-.012	**.813**	.031	.013	.214
MS-20	-.025	.185	-.021	.001	**.879**	.026	.016	-.002
MS-50	.075	-.008	-.014	.073	**.567**	-.008	-.040	.154
MS-28	-.006	-.044	.002	-.051	.069	**.911**	.017	-.083

MS-29	-.042	.202	-.020	.154	.042	**.654**	.020	.145
MS-35	-.047	.092	-.012	.085	-.008	**.891**	.010	.011
MS-36	.033	-.042	.027	.000	-.002	**.967**	.010	-.019
MS-37	.039	-.013	.017	-.010	-.036	**.862**	.011	.044
MS-38	.054	.079	-.026	.208	-.033	**.480**	-.021	.099
MS-21	.033	.010	.000	-.127	.003	-.008	**.896**	.025
MS-22	-.026	-.041	.040	.021	.028	.021	**.888**	.010
MS-23	.017	.033	.019	.019	-.004	.029	**.867**	-.012
MS-40	-.160	.272	.030	.322	.078	-.050	.017	**.469**
MS-43	.055	.325	-.032	.270	-.083	.041	.048	**.629**
MS-44	.040	-.067	-.002	-.028	.170	.011	.000	**.779**
MS-45	.044	.068	-.015	.071	-.034	.048	-.076	**.698**
MS-46	.007	.091	-.005	.257	-.050	-.219	.035	**.487**
MS-47	-.106	-.066	.029	-.121	.113	.043	-.019	**.884**
MS-48	-.092	-.011	-.017	-.067	.153	-.045	.018	**.881**

Figure 1. Literature-based theoretical model. Sexual orientation codes are as follows: bisexual men (1), gay men (2); + on an arrow indicates a positive influence, - on an arrow indicates a negative influence; for the internalized homophobia variables, O indicates "toward others," and S indicates "toward oneself".

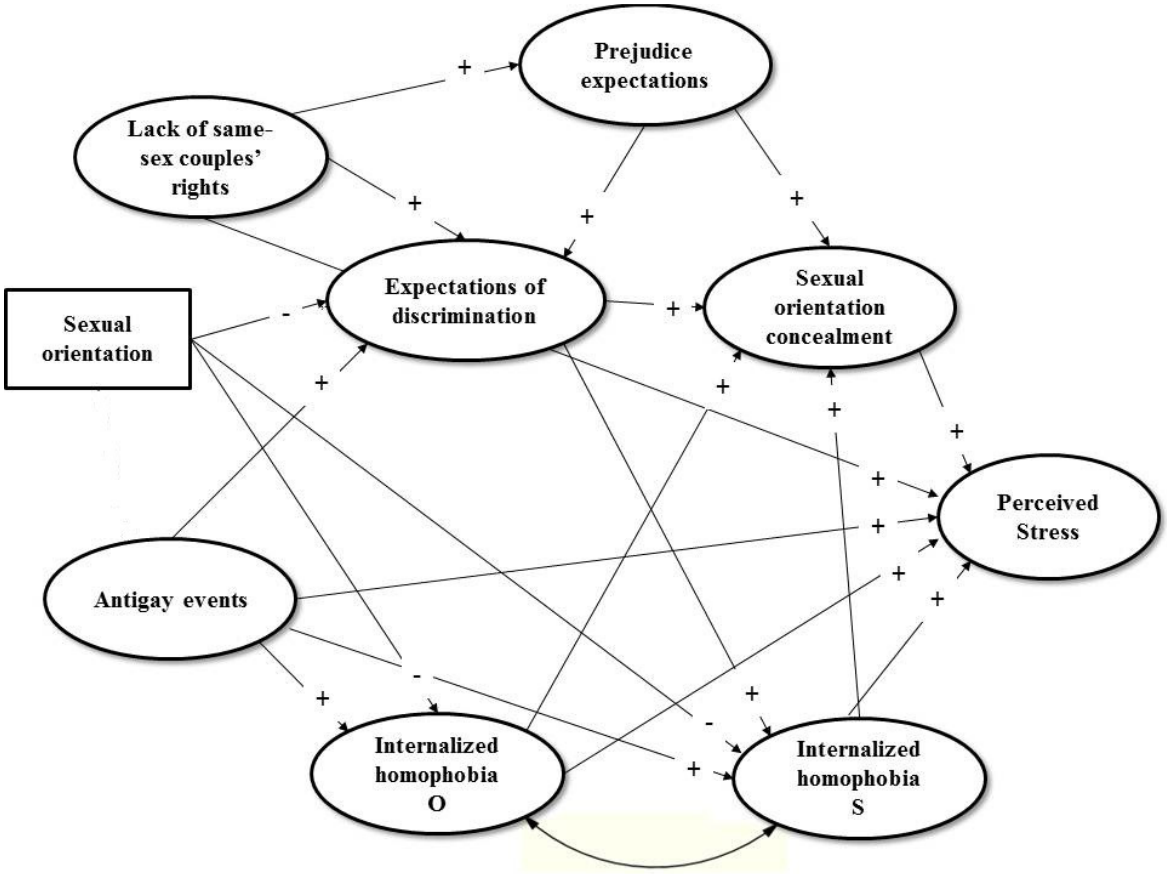

Figure 2. Structural Equation Model – Sexual orientation, minority stressors, and stress perception. ** p < .01, ** p < .001; Sexual orientation codes are as follows: bisexual men (1), gay men (2); for the internalized homophobia variables, O indicates "toward others," and S indicates "toward oneself." The loading of the joy dimension is positive because the scores of the various indicators were inverted to assess the *lack of joy*. This was performed in accordance with the recommendations of Levenstein et al. (1993) and Fliege et al (2005).

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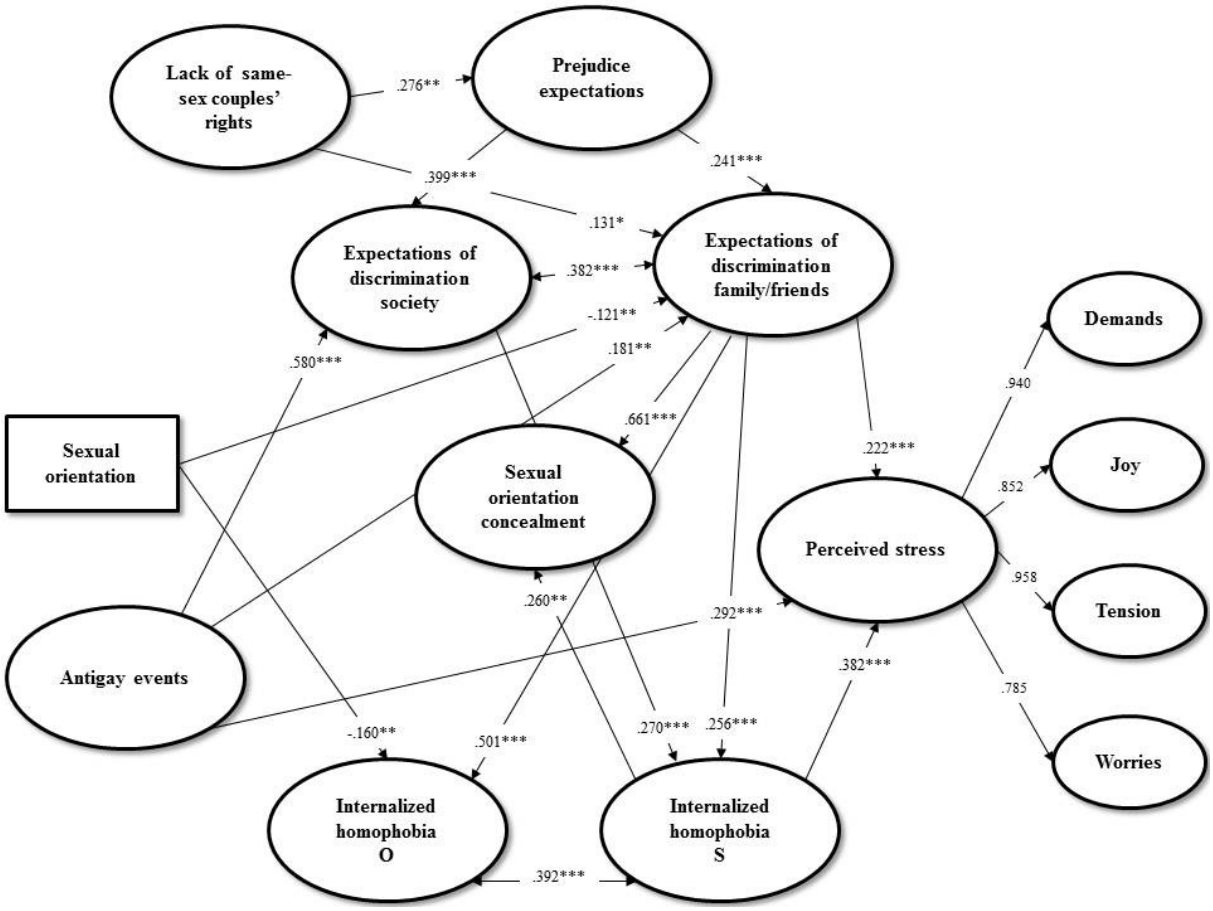

4.6 Minority Stressors are Associated with Lower CD4+ Cells Count, Greater Viral Load, and Depression in Two Samples of Italian HIV-Positive Gay and Bisexual Men

Norcini Pala, A., Steca, P., Levenstein, S., Varani, S., Calza, L., Colangeli, V., Cascavilla, A., Magistrelli, E., Viale, P.

Abstract

Minority stress is a form of psychosocial stress caused by the manifestations of sexual stigma. These *minority stressors* may negatively influence the well-being of gay and bisexual men directly. Additionally, they may act indirectly by increasing stress and cortisol levels, thereby impairing the immune system and promoting depression. Minority stressors might further threaten the health of HIV-positive individuals. In this work, we investigated the association of three minority stressors with biomarkers of HIV progression and depression in two samples of HIV-positive gay and bisexual Italian men. In addition, the roles of perceived stress and salivary cortisol were investigated. Study 1 (N=120) was conducted to test the associations between enacted sexual stigma, expectations of discrimination from one's family, and internalized homophobia towards oneself with CD4+ cell count, viral load, and depression. Internalized homophobia towards oneself and enacted sexual stigma were correlated with biomarkers of unfavorable HIV-progression and depression. Furthermore, expectations of discrimination from one's family were indirectly correlated with lower CD4+ cell count. In Study 2 (N=56), the roles of perceived stress and cortisol were also evaluated. Internalized homophobia was correlated with salivary cortisol. Enacted sexual stigma and expectations of discrimination from one's family were correlated with cortisol through perceived stress. Lastly, cortisol was associated with biomarkers indicative of the poorest HIV-progression and with increased levels of depression. Taken together, the minority stressors investigated here might impair the mental and physical health of HIV-positive individuals.

Key words: Internalized homophobia; Expectations of discrimination; Enacted sexual stigma; Stress; HIV progression; Salivary cortisol; Depression

4.6.1 Introduction

Minority stress is a psychosocial form of stress caused by the manifestations of sexual stigma. It adds to "general stress" (the type of stress that everyone may experience, irrespective of their minority or majority status), threatening the well-being of the members of sexual minority groups, such as gay and bisexual men. Indeed, the manifestations of sexual stigma, or *minority stressors,* increase the risk of mental disorders such as depression (Meyer, 1995, 2003). Schwartz and Meyer (2010) claimed that this might be due to the direct and indirect effects of minority stressors on mental health, namely by causing increased stress. Hence, physical health might also be at risk as perceived stress is associated with immune system impairment (e.g., Wüst et al., 2000). Based on these premises, minority stressors may be considered risk factors for HIV-positive gay and bisexual men. Therefore, as a result, they may be at increased risk for depression (see Rabkin, 2008) and immunosuppression (see Wüst et al., 2000). Furthermore, depression reduces the compliance with antiretroviral therapy (Rabkin, 2008), and this may aggravate a complex and already compromised health condition. The present work aims to investigate the association of minority stressors with physical and mental health in two samples of gay and bisexual HIV-positive individuals.

4.6.1.1 Manifestations of sexual stigma: The minority stressors

Minority stressors are chronic and stable as they are deeply rooted in discriminatory social processes. They can also be defined as *distal* or *proximal* in terms of their relationship with the self (Meyer, 1995, 2003). Proceeding from distal to proximal, Meyer described the enacted sexual stigma, expectations of discrimination, concealment of sexual orientation, and internalized homophobia. Recently, three of

these minority stressors have been found to be associated with greater perceived stress (Norcini Pala, Dell'Amore, Steca unpublished manuscript). Namely, "enacted sexual stigma" consists of physical and/or verbal manifestations of the stigma, such as verbal jokes and physical harassment. These events, in their turn, may promote expectations of future discrimination, which is the second minority stressor considered in this work. More precisely, we focus on "expectations of discrimination from one's family" because, unlike "expectations of discrimination from society (e.g., physicians, colleagues, and workplace)," it was found to be associated with greater perceived stress. This stressor consists of the individual expecting to be discriminated against by the members of his own family. Lastly, "internalized homophobia" is the stressor that is most proximal to the self and embodies the introjection of societal negative attitudes towards homosexuality. In line with Herek (2004, 2009), internalized homophobia should be considered in two dimensions. Namely, internalized homophobia is directed towards homosexuality in others, and internalized homophobia is directed towards homosexual features in oneself (see also Shidlo, 1994). Internalized homophobia may occur because the homophobic attitudes have been embedded long before individuals realize their own sexual orientations. Therefore, the negative attitudes that were initially directed towards others could be later directed towards oneself. Furthermore, growing up in a homophobic environment (e.g., society or family) may be a risk factor for internalized homophobia, and this can explain the association between expectations of discrimination from one's family and internalized homophobia towards oneself. On the one hand, the enacted sexual stigma itself may promote internalized homophobia, for the victims of homophobic aggressions might show discomfort with their own sexual orientation (Meyer, 1995).

4.6.1.2 A psychosocial and physiological hypothesis

The three minority stressors described above could also affect mental health through perceived stress (Schwartz & Meyer, 2010). This means that these minority stressors may act through undercover physiological pathways, namely by increasing cortisol production. Perceived stress, indeed, is associated with increased cortisol levels (Wüst et al., 2000), which are associated with depression (e.g., Zunszain et al., 2011) and a more severely impaired immune system (Meuleman & Katz, 1985). Furthermore, it has been demonstrated that cortisol promotes HIV replication (Goodkin et al., 1996; Markham, Salahuddin, Veren, Orndorff, & Gallo, 1986). Additionally, it activates the enzyme TDO (TRY-2,3-dioxygenase) that causes tryptophan degradation and reduces serotonin, thereby causing depression (Zunszain et al., 2011). Kynurenine, which is the tryptophan metabolite produced in its depletion pathway, has an immunosuppressive effect (Bauer, Jiga, Chuang, Randazzo, Opelz, & Terness, 2005). Therefore, assuming that minority stressors might increase cortisol levels, there could be a "covert" pathway through which depression risk is increased, and the immune system is severely impaired.

4.6.1.3 Aims

This work aimed to test the associations between enacted sexual stigma, expectations of discrimination from one's family, and internalized homophobia toward oneself and lower CD4+ cell count, greater viral load (namely, a greater amount of biomarkers of unfavorable HIV progression), and depression in two samples of Italian gay and bisexual HIV-positive men. The roles of perceived stress and cortisol in modulating such relationships were also investigated. To the best of our knowledge, this is the first work conducted to examine a psychoimmunological model of the underlying

relationships between minority stressors, depression, and biomarkers of HIV progression. Two cross-sectional studies were conducted: Study 1 was conducted online to test the association of minority stressors with depression and self-reported biomarkers of HIV progression (CD4+ cells count and viral load). The association between depression and such biomarkers was also tested. Study 2 was conducted offline to examine the mediating roles of perceived stress and cortisol regarding the effects of minority stressors on mental and physical health. Overall, our expectations were to find that the three minority stressors were intercorrelated and significantly associated with lower CD4+ cell count, greater viral load, and depression. Minority stressors were also expected to correlate with perceived stress and salivary cortisol, which were also expected to be intercorrelated. In summary, the association of minority stressors with biomarkers of HIV progression and depression was examined. More precisely, we investigated their direct and indirect associations by examining the potential mediation by perceived stress and cortisol (see Schwartz & Meyer, 2010).

Study 1

4.6.2 Method

4.6.2.1 Participants and procedure

The participants (N = 120) were all Italian, HIV-positive gay (91.82%) and bisexual (8.18%) men with a mean age of 39.95 (*SD*= 9.86; ranging from 21 to 74) years. Participants' education included completion of junior high school (4.55%), high school diploma (51.82%), university degree (12.73%), master's degree (18.18%) and Ph.D. or other specialization (6.36 %; missing data 6.36 %). Of the entire group, 75 % (n = 90) of the individuals self-reported that they were undergoing ART

(AntiRetroviral Therapy), whereas 23.33 % self-reported that they were not currently undergoing ART; two subjects did not answer (1.67 %; see Table 1).

A non-probabilistic convenience sampling procedure was adopted, and recruitment took place between September 2010 and August 2011 and was web-based. A message was posted on web-sites and forums related to HIV/AIDS and provided the following information: a general description of the study, the inclusion criteria (HIV diagnosis and age over 18), and the authors' academic affiliation. Questionnaires were completed and submitted online to an ad-hoc e-mail account specifically used for this study. In each phase of the study, participants' privacy and anonymity were respected; additionally, participants were informed that the survey was voluntary, and they had to declare that they were over 18 years of age.

4.6.3 Measures

Minority stressors were assessed using three scales developed in Italian and validated in a previous unpublished work. The *enacted sexual stigma* was assessed using 3 items ("I have been verbally attacked, "I have been physically attacked," and "I have been discriminated against**"**) to determine the frequency of enacted sexual stigma experienced by participants in the past. The items were rated on a Likert scale from 1 (*Never*) to 5 (*Always*) (loadings ranged from .74 to .81 and α=.71). *Expectations of discrimination from one's family* was assessed with 3 items worded to capture the expectations of being discriminated against by family members (e.g., "I don't think my family would accept me," and "As a homosexual/bisexual, I am afraid of being discriminated against by my family members"). Participants rated the items on a 5-point scale from 1 (*Completely disagree*) to 5 (*Completely agree*) (loadings ranged from .56 to .72 and α=.85). *Internalized homophobia towards oneself* was composed

of 6 items designed to assess an individual's homophobic attitudes directed towards the self (e.g., "I avoid any physical contact with people of my sex because I find it embarrassing," "I wish I weren't homosexual/bisexual," "My sexual orientation makes me feel really bad"). Items were rated from 1 (*Completely disagree*) to 5 (*Completely agree*) (loadings ranged from .58 to .98 and α=.90).

Depression was assessed using the PHQ-9 (Patient Health Questionnaire; Kroenke, Spitzer and Williams, 2001), which is composed of 10 items that incorporate the diagnostic criteria of depression. The participants were asked to rate themselves on a scale from 0 (*Not at all*) to 3 (*Nearly every day*) to evaluate the frequency of symptoms experienced in the past 2 weeks (loadings ranged from .65 to .88, α = .90).

Biomarkers of HIV progression (self-reported) were viral load and CD4+ cell count; based on their most recent blood test, the participants reported the values of their biomarkers using methods in-line with those of previous studies that used the same web-based approach (Halkitis et al. 2003; Kalichman, Rompa and Cage, 2000). The participants also self-reported whether they were currently taking HAART (1 *Yes* /2 *No*).

4.6.4 Data Analysis

SPSS 15.0 (SPSS Inc. Chicago, IL, 2006) was used to assess the distributions of the variables. Skewness and kurtosis values lower than |1| indicated a normal distribution, whereas values greater than |1| indicated a non-normal distribution. Several variables violated the normality assumption, and they were thus treated as ordinal. Mplus 6.1 (Muthén and Muthén, 2010) was used to perform Structural Equations Modeling (SEM). In both SEMs, the Weighted Least Square Method (WLSMV) was used for the ordinal, continuous, and binary natures of the variables,

together with the small sample size (Flora and Curran, 2004; Finney and DiStefano, 2006). Goodness-of-fit indexes included the Tucker-Lewis Incremental fit index (TLI; Tucker and Lewis, 1973), the Comparative Fit Index (CFI; Bentler, 1990), RMSEA and the χ^2/df ratio (Crowley and Fan, 1997). CFI and TLI scores ≥ .95 indicated good fit, while scores ≥ .90 indicated sufficient fit. A RMSEA score ≤.05 indicated a good fit, whereas a score ≤ .08 indicated a sufficient fit of the model. A χ^2/df ratio ≤5 indicated a good fit for the model (Bollen, 1989; Crowley and Fan, 1997; Hu and Bentler, 1999; Schermelleh-Engel, Moosbrugger and Muller, 2003).

4.6.5 Results

A Structural Equation Model (SEM) was performed to test the association of enacted sexual stigma, expectations of discrimination from one's family, and internalized homophobia towards oneself with CD4+ cell count, viral load, and depression. The model resulted in very good fit indexes (CFI/TLI .98/.98, RMSEA = .05, χ^2/df=1.52) and has been graphically represented in Figure 1 (non-significant results were omitted to improve the readability of the figure). In contrast with our hypothesis, only expectations of discrimination from one's family were associated with internalized homophobia towards oneself, and no other intercorrelations were observed among minority stressors. Internalized homophobia towards oneself and enacted sexual stigma were correlated with depression and with biomarkers of unfavorable HIV progression. More precisely, participants who had experienced homophobic aggression showed greater viral loads, whereas greater internalized homophobia was associated with lower CD4+ cell count. Furthermore, expectations of discrimination from one's family were indirectly associated with lower CD4+ cell

count; that is, this association was mediated by internalized homophobia (β = -.13, p = .04).

4.6.6 Discussion

Minority stressors may affect the mental and physical health of gay and bisexual seropositive men, thereby increasing their risks of depression and of developing biomarkers of unfavorable HIV progression. Enacted sexual stigma, expectations of discrimination from one's family, and internalized homophobia towards oneself were previously found to correlate with greater perceived stress (Norcini Pala, Dell'Amore, & Steca, unpublished manuscript; see also Schwartz and Meyer, 2010). Subsequent investigations have shown that these factors are associated with impaired immune system functioning (e.g., Watts, 2005; Schlotz et al., 2011) and depression (Zunszain et al., 2011) in a sample of gay and bisexual HIV-positive Italian men. These associations might be due to greater perceived stress (Schwartz and Meyer, 2010). Internalized homophobia towards oneself correlates with lower CD4+ cell count and depression. Because this stressor is strictly associated with the self (Meyer, 1995), it should be considered as the more insidious internal stressor (Meyer, 2003). For instance, individuals who experienced self-threatening stressors reported greater levels of stress (e.g., Dickerson et al., 2004). These results may confirm that minority stressors are harmful and that internalized homophobia towards oneself may be a more influential minority stressor due to its "position" with respect to the self. The observed mediation of internalized homophobia could reinforce the hypothesis that internalized homophobia is extremely harmful. As expected, expectations of discrimination and internalized homophobia were interrelated. This might be in line with the hypothesis that individuals who grow up

in a homophobic family environment might expect to be discriminated against by their family members. Additionally, they could also have encountered and internalized homophobic attitudes in their childhood or adolescence (Herek, 2009).

Viral load was associated with enacted sexual stigma, perhaps due to the mediating effect of stress. For instance, in response to stressful events, elevations in the circulating levels of cortisol, norepinephrine and epinephrine have been observed (Romero and Butler, 2007). Cortisol could reduce immune system functioning, while norepinephrine and epinephrine could promote HIV replication (Antoni, 2003; Cole, 2008). However, these statements require caution.

No association between depression and viral load was found. This result might be due to the lack of an assessment of compliance with treatment regimens. In fact, depression is thought to reduce compliance, which may, in turn, affect viral load.

Study 2

4.6.7 Method

4.6.7.1 Participants and procedure

The participants (N = 56) were HIV-positive gay (89.47%) and bisexual (10.53%) Italian men. Their mean age was 36.40 (SD = 8.01; ranging from 24 to 55) years, and their education included junior high school (19.30%), high school diploma (43.86%), university degree (10.52%), master's degree (14.04%) and Ph.D. or other specialization (8.77%); two participants did not provide data (3.51%). Some were undergoing HAART (59.65%), some were not undergoing HAART (35.09%), and three did not provide this information (missing data 5.26 %; (see Table 1).

The participants were HIV-positive patients followed by the Infectious Diseases Operative Unit (S. Orsola-Malpighi Hospital, Bologna, Italy) and were recruited over a period of 5 months. A randomized sampling procedure was adopted: five patients (out of a list of 20) were randomly selected using an SPSS algorithm from the weekly schedule of blood screening appointments. These participants were contacted by phone by the first author of this work one week before their scheduled blood test (HIV-positive patients take blood tests 3 times per year). During the phone call, the recruiter introduced the general aims of the study ("The study aims to evaluate psychological factors that might promote HIV progression"). Additionally, the voluntary nature of participation was constantly stated and emphasized. The participants received, read, and signed informed consent forms on the day of the blood test. Within the informed consent, the following information was provided: "Participation is voluntary; you can decide to retire from the study. The data gathered will be kept strictly confidential and anonymously analyzed." Individuals who did not participate were reassured that there would not be consequences and that the doctors of the unit would continue seeing them. Lastly, all the participants were invited to request an interview with the first author of this work for further information. The participants completed the questionnaires and signed them on the day of their medical appointment (generally after 2 weeks after the blood test). The patients were informed that their CD4+ cell count and viral load would be gathered directly from their clinical records and that, to ensure anonymity, a code would be used to match questionnaires with data on the biomarkers of HIV-progression. This study was approved by the S. Orsola Malpighi Ethical Committee.

4.6.8 Measures

Minority stressors were assessed with the instrument used in Study 1. The loadings of the items of *enacted sexual stigma* ranged from .44 to .91 (α=.72). The items related to *expectations of discrimination from one's family* ranged from .66 to .95 (α=.74), whereas the items of *internalized homophobia towards oneself* showed loadings ranging from .47 to .94 (α=.90).

Depression was assessed with PHQ-9 (Patient Health Questionnaire; Kroenke, Spitzer and Williams, 2001), which showed loadings ranging from .34 to .82 (α = .85).

Perceived Stress was assessed with the Recent (over the last 4 weeks) Perceived Stress Questionnaire (Levenstein et al., 1993), which was composed of 7 dimensions and 30 items on a 4-point scale ranging from 1 (*Almost never*) to 4 (*Usually*). In this study, we adopted the Fliege et al. (2005) brief version, which was composed of one second-order factor (perceived stress) together with four first-order factors (worries, tension, lack of joy, and demands; 20 items). We opted for this version to reduce the complexity of the model (i.e., the number of factors) because of the small sample size. The loadings of the latent variables of the second-order factor ranged from .80 to .94.

Biomarkers of HIV progression were gathered by consulting the clinical records of each patient. The biomarker measurements were performed on the day of blood test, when the questionnaires were delivered and a saliva sample was provided by each of the patients. The participants were also instructed to specify whether they were currently undergoing HAART (1 *Yes* /2 *No*).

Salivary cortisol was determined using an ELISA kit (Pantec s.r.l. Turin, Italy). The participants each provided a sample of saliva gathered just after waking on

the day of their blood test. They were instructed to obtain the sample before they brushed their teeth and before they ate breakfast. The saliva samples were collected in urine containers (patients generally had containers, and if they did not, they were asked to take a free container from the pharmacy). Our intent was to investigate the association of psychological constructs with cortisol production soon after waking (within 15 minutes of waking). Cortisol production may significantly vary during the day (or even during waking), but our intent was not to assess daily cortisol production dysregulation. Additionally, if multiple saliva samples were requested, patients' adherence to this procedure might not have been accurate, especially when their motivation was low. We opted for a single sample taken at a single time point after consulting the scientific literature; the same procedure was used in previous studies (Burton et al., 1996; Harenstam and Theorell, 1990; McBurnett et al., 2000; Steptoe et al., 1998).

4.6.9 Data Analyses

SPSS 15.0 (SPSS Inc. Chicago, IL, 2006) was used to assess the variables' distribution. Skewness and kurtosis values lower than |1| indicated a normal distribution, whereas values greater than |1| indicated a non-normal distribution. Several variables violated the normality assumption and were thus treated as ordinal. Structural Equation Modeling (SEM) was performed using Mplus 6.1 (Muthén and Muthén, 2010). The Weighted Least Square Method (WLSMV) estimator was used because of the mixed nature of the variables (ordinal, continuous, and binary) and the small sample sizes (Finney and DiStefano, 2006; Flora and Curran, 2004). To reduce possible sample size bias, a bootstrap was also performed (Muthén and Muthén, 2010). Goodness-of-fit indexes included the Tucker-Lewis Incremental fit

index (TLI; Tucker and Lewis, 1973), the Comparative Fit Index (CFI; Bentler, 1990), RMSEA and the χ^2/df ratio (Crowley and Fan, 1997). CFI and TLI scores ≥ .95 indicated good fit, while scores ≥ .90 indicated sufficient fit. A RMSEA score less than or equal to .05 indicated a good fit, while a score less than or equal to .08 indicated a sufficient fit of the model. A χ^2/df ratio lower than 5 indicated a good fit for the model (Bollen, 1989; Crowley and Fan, 1997; Hu and Bentler, 1999; Schermelleh-Engel, Moosbrugger and Muller, 2003).

4.6.10 Results

The model tested resulted in a sufficient fit (CFI/TLI .91/.91, RMSEA = .04, χ^2/df=1.08), and significant associations are graphically represented in Figure 2 (non-significant associations were excluded to improve the readability of the model). The association between expectations of discrimination from one's family and internalized homophobia towards oneself was confirmed. Those individuals with greater expectations of discrimination from their family and those who have experienced homophobic aggression (e.g., physical or verbal harassment) showed greater perceived stress. In addition, as hypothesized, perceived stress was associated with greater salivary cortisol. Of the minority stressors tested, internalized homophobia towards oneself showed a direct association with salivary cortisol. Conversely, expectations of discrimination were indirectly associated with salivary cortisol through both internalized homophobia ($\beta = .21$, $p < .01$) and perceived stress ($\beta = .26$, $p < .01$). Notably, enacted sexual stigma, perceived stress, and salivary cortisol were all associated with depression. In line with our hypothesis, salivary cortisol and viral load negatively correlated with CD4+ cell count, whereas cortisol was also associated with greater viral load. Expectations of discrimination, through

perceived stress and salivary cortisol (β = .49, p < .001), indirectly correlated with lower CD4+ cell counts (β = -.12, p = .04) and increased depression (β = .13, p = .05). Lastly, depression was not associated with biomarkers of HIV-progression.

4.6.11 Discussion

Minority stressors are associated with poor mental and physical health in gay and bisexual HIV-positive men. The enhanced cortisol concentration that results from greater perceived stress (Wüst et al., 2000) may be the link between the observed associations (Schwartz and Myer, 2010). Cortisol can impair the immune system and promote depression by causing tryptophan depletion (Zunszain et al., 2011). Hence, minority stressors might worsen the mental and physical health of HIV-positive individuals by generating greater perceived stress and cortisol. This result was observed for enacted sexual stigma (e.g., physical or verbal harassment) and expectations of discrimination from one's own family. Internalized homophobia towards oneself is directly associated with cortisol levels. This result might confirm that internalized homophobia is extremely stressful and harmful (Meyer, 1995, 2003) and may have the same consequence as perceived stress (greater cortisol), although individuals may feel not "stressed" (see also Dickerson et al., 2004).

Expectations of discrimination from one's family might increase cortisol through two likely factors: perceived stress and internalized homophobia towards oneself. Its association with internalized homophobia could also be interpreted as the consequence of having experienced a homophobic and hostile familial environment (Herek, 2009; Meyer, 1995 2003).

Perceived stress is associated with salivary cortisol (Romero & Butler, 2007) and a greater level of biomarkers of unfavorable HIV progression (Antoni, 2003;

Cole, 2008). Likewise, according to Zunszain et al. (2011), cortisol could also trigger the depletion of tryptophan, which in turn promotes depression. Hence, we hypothesize that minority stressors may cause physiological reactions to stress that have potentially detrimental effects on health.

Interestingly, enacted sexual stigma shows a direct association with depression as the association between these factors is not mediated by perceived stress or cortisol (see Schwartz and Meyer, 2010). Although further investigation is needed to draw robust conclusions, we hypothesize that traumatic experiences might contribute to the development of implicit depressive cognitions (Johnson, Benas, and Gibb, 2011). Lastly, depression is not associated with biomarkers of HIV-progression. However, this might due to the small sample size.

Our findings provide confirmation of the model proposed by Schwartz & Meyer (2010), in which it is stated that stress might not be the only pathway through which minority stressors affect well-being. However, cortisol still plays a central role.

Because of the cross-sectional nature of the study and the small size, we used caution in drawing conclusions and generalizing the results. Future investigations may help in understanding possible alternative pathways by examining, for instance, implicit and explicit factors.

4.6.12 General discussion

The studies discussed in this work provide confirmation of the models proposed by Meyer, (1995, 2003) and Schwartz and Meyer (2010) with respect to minority stressors' actions on health. Increased depression and impaired immune system functioning may be the consequence of minority stressors that may act directly and

indirectly through physiological pathways (e.g., Cole, 2008; Segerstrom and Miller, 2004; Zunszain et al., 2011). Such consequences are extremely harmful for HIV-positive individuals. In fact, evidence confirms that HIV positive individuals are at greater risk of depression (Rabkin, 2008). Minority stressors, then, may aggravate this condition. Likewise, given that HIV impairs the immune system, the immunosuppressive actions of cortisol produced in reaction to minority stress is detrimental.

The minority stressors examined need future investigation, especially in clinical contexts. Taken together, because of their negative effects, minority stressors should be assessed in the clinical context of HIV. An effective management might comprise psycho-educational interventions to manage stress, which have been shown to produce positive effects (Brown and Vanable, 2011). Stress-reduction interventions, which would limit the effects of stress and cortisol on mental and physical health, would also be beneficial (Balfour, Kowal and Silverman, 2006; Brown et al., 2011; Brown and Vanable, 2011; Cruess, Antoni and Hayes, 2002). Lastly, because depression might reduce compliance and thus contribute to worsening clinical profiles (Balfour, Kowal and Silverman, 2006), depression should be routinely assessed. Although we did not find any significant association between depression and viral load or CD4+ cell count, the literature shows that depression may severely impair health (e.g., Rabkin, 2008).

The limitations of the present work should be overcome with a longitudinal study that we are currently undertaking. With this study, we aim to understand directionality of the observed associations.

However, it should be noted that because of the cross-sectional nature of these studies, we cannot draw any conclusion on regarding the directionality of the

relationships assessed in this work. Instead, we provide possible explanations that are based on previously published literature. Additionally, a larger sample size should be used.

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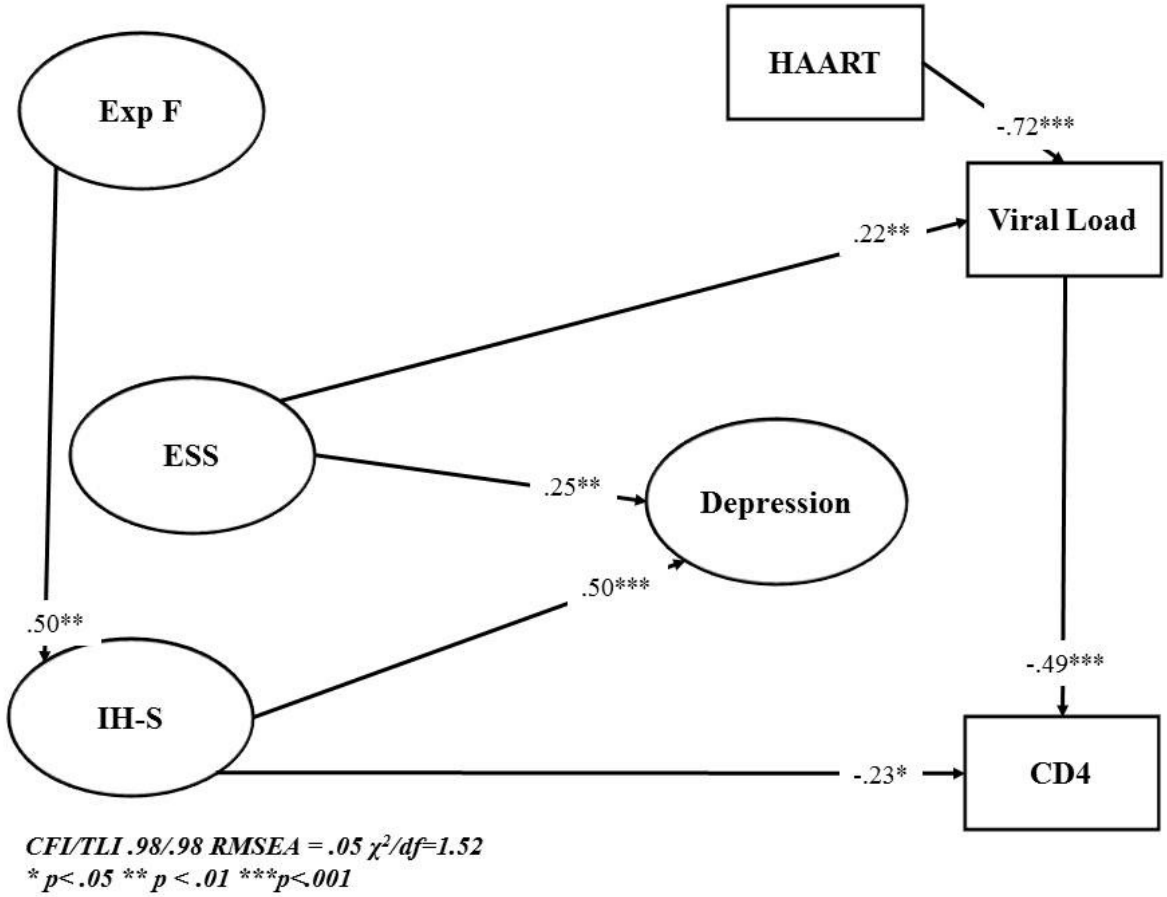
Table 1 Descriptive statistics: participants' age, viral load, CD4+ cell count, and participation in HAART

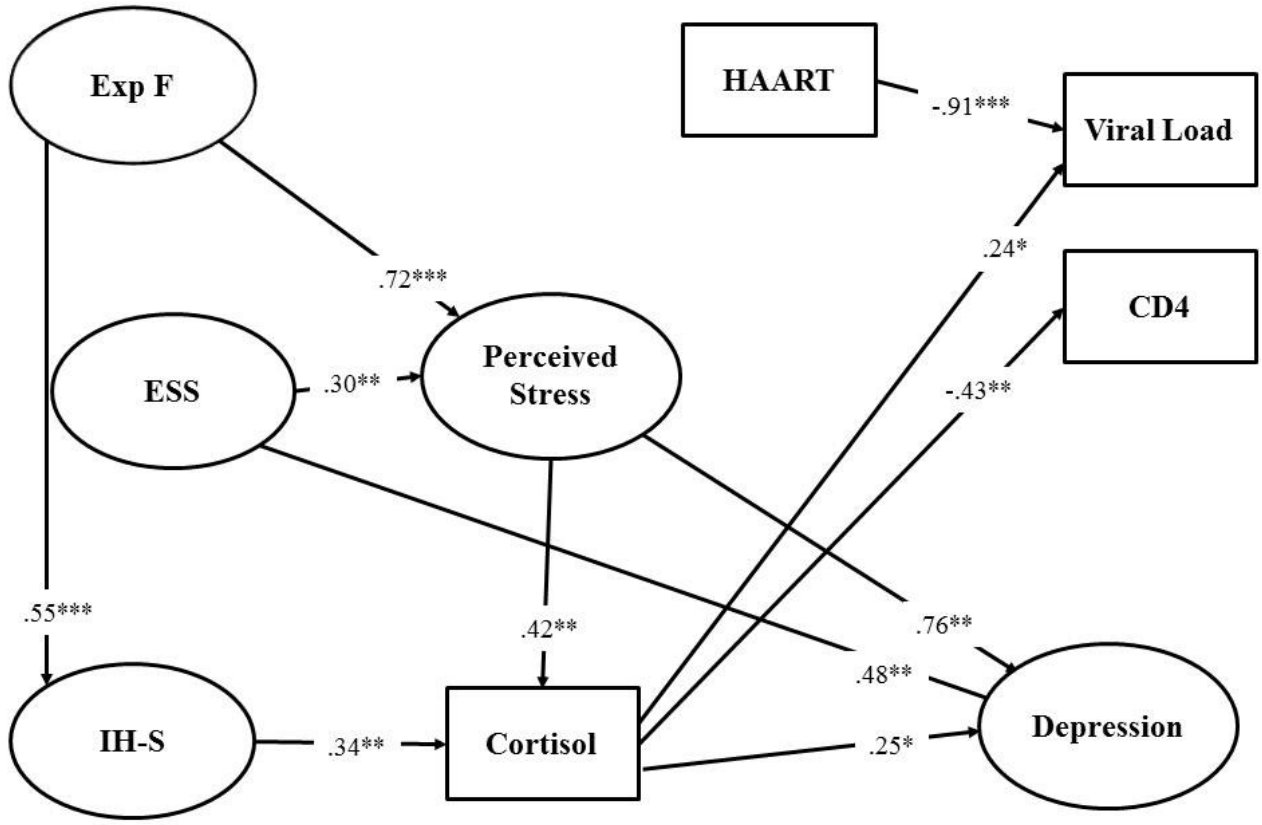
	Study 1	Study 2
Mean age	39.95 (*SD* = 9.86) from 21 to 74 years	36.40 (*SD* = 8.01) from 24 to 55 years
Mean viral load	7063.82 (*SD* = 17974.71) Undetectable load (<50) 69.10%	19134.38 (*SD* = 38500.93) Undetectable load (<50) 50.91%
Mean CD4+ cell counts	574.13 (*SD* = 243.00)	633.11 (*SD* = 303.41)

Figure 6 SEM – Association of minority stressors with biomarkers of HIV progression and depression (Study 1)



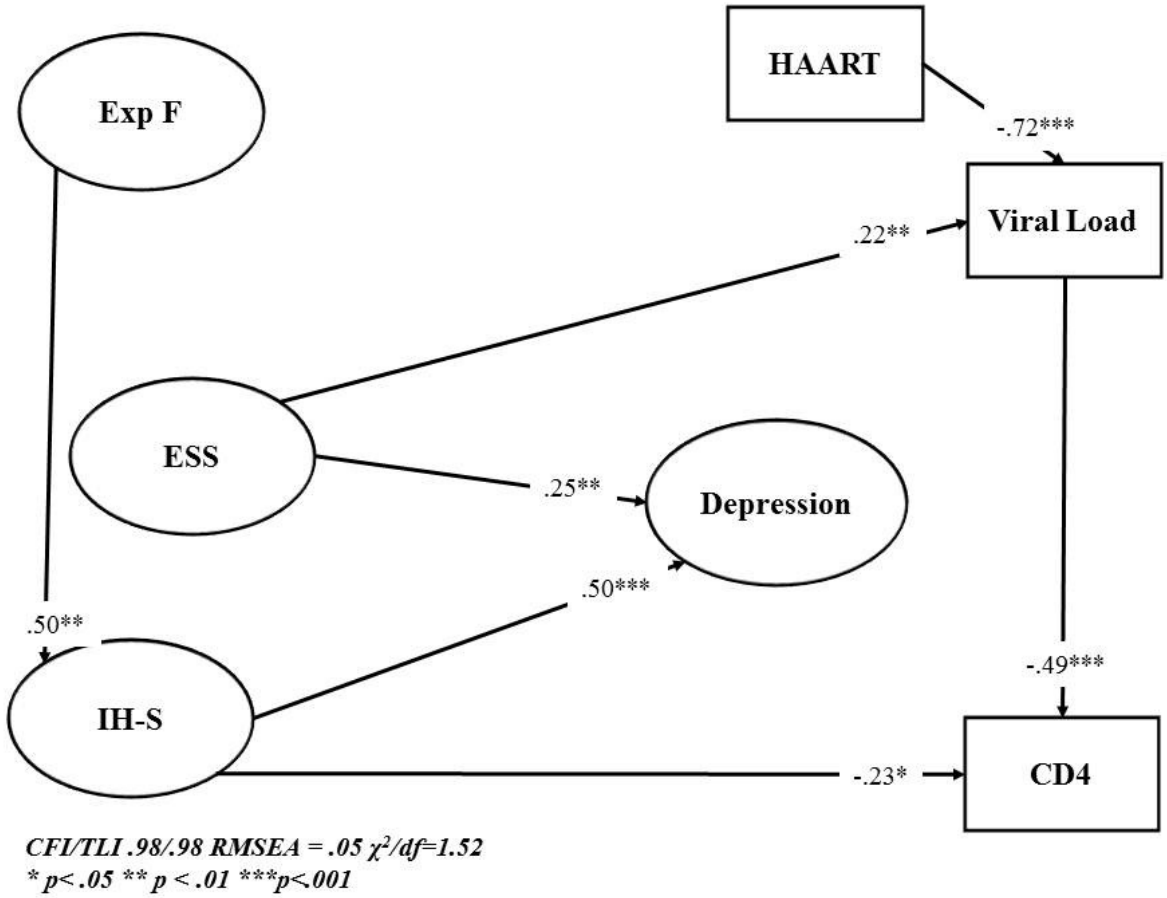
Exp F: Expectations of discrimination from one's family; ESS: Enacted sexual stigma; IH-S: Internalized Homophobia towards Oneself; HAART: (1) HAART naïve / (2) under HAART treatment.

Figure 2 SEM - Association of minority stressors with perceived stress, salivary cortisol, biomarkers of HIV progression, and depression (Study 2)



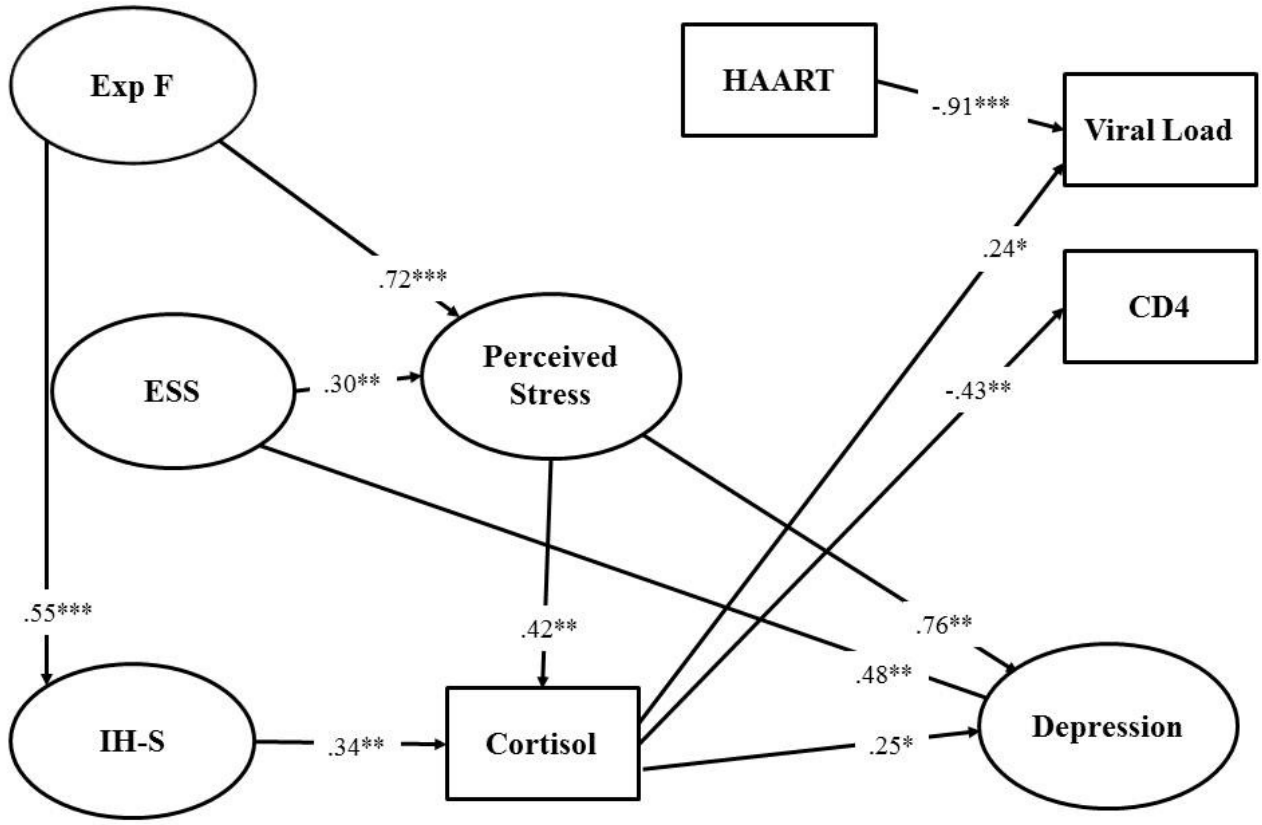
Exp F: Expectations of discrimination from one's family; ESS: Enacted Sexual Stigma; IH-S: Internalized Homophobia towards Oneself; HAART: (1) HAART naïve / (2) under HAART treatment; Cortisol: single measure of salivary cortisol.

Figure 7 SEM – Association of minority stressors with biomarkers of HIV progression and depression (Study 1)



Exp F: Expectations of discrimination from one's family; ESS: Enacted sexual stigma; IH-S: Internalized Homophobia towards Oneself; HAART: (1) HAART naïve / (2) under HAART treatment.

Figure 2 SEM - Association of minority stressors with perceived stress, salivary cortisol, biomarkers of HIV progression, and depression (Study 2)



Exp F: Expectations of discrimination from one's family; ESS: Enacted Sexual Stigma; IH-S: Internalized Homophobia towards Oneself; HAART: (1) HAART naïve / (2) under HAART treatment; Cortisol: single measure of salivary cortisol.

4.7 HIV Adherence Self-efficacy: An Emerging Influential Psychological Construct in the Era of HAART

* **Norcini Pala, A., * Steca, P., *** Johnson, M.O., ** Varani, S., ** Magistrelli, E., ** Colangeli, V., ** Cascavilla, A., ** Salvadori, C., ** Calza, L., ** Viale, P.

* Psychology Department, Milano-Bicocca University, Milan, Italy

** Infectious Diseases Dpt. Sant'Orsola-Malpighi Hospital, Bologna, Italy

*** Center for AIDS Prevention Studies, University of California San Francisco, San Francisco, CA, USA

Abstract

Antiretroviral Therapy (ART) slows the progression of HIV if patients strictly adhere to their treatment regimens, yet rates of ART adherence among people with HIV are suboptimal. Among many other factors related to ART adherence, individuals must perceive themselves to be capable of adherence, that is, they must have the self-efficacy needed for adherence. Thus, belief in the capability to engage in healthy behaviors related to HIV management has been shown to predict greater adherence and better clinical outcomes. In this paper, the psychometric properties of the Italian version of the HIV Adherence Self-Efficacy Scale (HIV-ASES) and its association with depression, ART adherence, and viral load were investigated. Two samples of HIV-positive patients on ART were recruited (Study 1-N=119 and Study 2-N=95). In Study 1, three highly correlated factors were extracted through exploratory factor analysis: (1) adherence self-efficacy, (2) integration, and (3) perseverance. Within two SEMs (Studies 1 and 2), a second-order factor, labeled "Adherence self-efficacy," was identified, and it was found to be significantly associated with lower levels of depression, greater compliance, and lower HIV viral loads after four months. The findings suggest that HIV adherence self-efficacy assessment in the clinical context of HIV might be helpful in targeting patients who need specific attention in order to reduce non-compliance and promote better clinical outcomes, namely lower viral loads and lower levels of depression.

Keywords: HIV; HAART; Adherence, Self-efficacy; Depression; Compliance

4.7.1 Introduction

Patients treated with ART (Antiretroviral Therapy) show slower rates HIV progression, which is currently considered a chronic and lifelong managed illness (Siegel, & Lekas, 2002). The extent to which individuals adhere to their treatment plans and medical appointments largely determines their clinical outcomes. Thus, patient behaviors are central to the success of the treatment process. Psychologically, individuals must perceive themselves to be capable of enacting behaviors related to HIV management. In fact, there are circumstances in which one may feel unable to or uncomfortable with taking ART (e.g., in front of friends or in contexts in which patients did not wish to reveal their serostatus), and in addition, if illness management interferes with patients' daily routines, adherence may be significantly reduced. The management of HIV infection consists of many different behaviors and not just of "medicine taking," e.g., following a healthy diet and healthy lifestyle. The degree to which patients follow medical and behavioral prescriptions might be defined as "adherence," whereas with the term "compliance," we refer to the extent to which patients take prescribed medicines. It is quite intuitive to consider compliance to be a part of the adherence construct. However, all the prescriptions play a part in determining patients' clinical outcomes. Also, the regularity of medical visits is important for an efficacious and continuous screening of the infection's progression. In sum, HIV diagnosis may change the daily lives of patients, who will have to make great efforts to manage it. In order to deal efficaciously with HIV infection, individuals must perceive themselves to be able to be adherent (Meichenbaum & Turk, 1987). This certainly plays an important role in slowing down HIV progression because it may predict greater adherence (Bangsberg, Acosta, Gupta et al., 2006; Paterson, Swindells, Mohr et al., 1989). Therefore, perceived self-efficacy could play a crucial role in determining effective HIV self-management (Bandura, 1989;

Johnson, Neilands, Dilworth et al., 2007). Task-specific self-efficacy (e.g., perceived self-efficacy related to perseverance in ART treatment; Rapley & Fruin, 1999) is especially important. This is also confirmed by the fact that perceived self-efficacy is associated with a lower risk of depression (Bandura, 1989), which is a very common mental disorder that, along with the disabling effect it has on one's life quality, has been proven to reduce adherence among HIV-positive individuals (Bhatia, Hartman, Kallen, Graham, & Giordano, 2011; Kroenke, Spitzer, & Williams, 2001; Halkitis, Parsons, Wolitski, & Remien, 2003). Also, HIV adherence self-efficacy might plausibly act indirectly on adherence by reducing depression. Johnson et al. (2007) developed a psychometric instrument (HIV-ASES; HIV Adherence Self-Efficacy Scale) that identified two latent dimensions underlying HIV adherence self-efficacy, namely integration (the treatment's integration into patients' daily lives) and perseverance (adherence to treatment regimens even when facing adversity). These factors are both extremely important for effective daily HIV self-management.

4.7.2 Aims

Due to its relevance and potential application in the context of HIV treatment, in this paper, the Italian version of HIV-ASES was validated, and its association with depression, compliance, and viral load was tested. In addition, whether HIV-ASES and ART adherence predicted lower viral loads at a four-month follow-up was also tested. This work is based on two studies conducted on two different samples of HIV-positive individuals who were treated with ART. Throughout the paper, we will refer to "Study 1" and "Study 2." First, the dimensionality of the instrument was evaluated, together with HIV-ASES's association with depression and viral load (Study 1). A negative association between HIV-ASES and depression and viral load was expected

(Bandura, 1999; Johnson et al., 2007); in addition, depression was expected to be associated with greater viral load because of its effect on compliance (Bhatia et al., 2011; Kroenke, Spitzer, & Williams, 2001; Halkitis et al., 2003; Figure 1). In Study 2, the factorial model of HIV-ASES was tested, and its association with depression, compliance, and viral load was verified. Lastly, HIV-ASES and compliance were tested as predictors of viral load after a four-month follow-up. As in Study 1, HIV adherence self-efficacy was expected to correlate inversely with depression and viral load, as well as positively with compliance, which was expected to be associated with lower viral loads (Johnson et al., 2007). Depression was instead expected to be associated with poorer compliance and consequently with higher viral loads (Bhatia et al., 2011; Kroenke, Spitzer, & Williams, 2001; Halkitis et al., 2003). Lastly, HIV-ASES and compliance were tested as predictors of lower viral load at follow-up (see Figure 2).

Study 1

4.7.3 Method

4.7.3.1 Participants and procedures

The participants (N = 119) were HIV-positive women (14.29%) and men (85.71%) who were treated with ART and recruited through the Internet (e.g., HIV-related websites, forums, and chat rooms). Their mean age was 41.54 years (SD = 9.67).

Recruitment occurred over one year (from September 2010), and participants' anonymity was achieved due to the web-based methodology adopted. The questionnaires were compiled and submitted to the first author's e-mail through the Internet. Because of the specific method adopted (online), participants' anonymity and privacy were respected. To begin compiling the questionnaires, participants self-

declared as being seropositive, over 18 years old, and in agreement with the terms and conditions of the study.

4.7.3.2 Measures

HIV adherence self-efficacy was assessed using the Italian version (edited by the authors of this paper) of the HIV-ASES (HIV Adherence Self-Efficacy Scale; Johnson et al., 2007). The instrument was composed of twelve items that were rated on an 11-point scale ranging from *Cannot do at All* (0) to *Moderately Certain Can Do* (5) to *Completely Certain Can Do* (10).

The presence of depressive symptoms during the prior two weeks was assessed through the PHQ-9 (Patient Health Questionnaire) (Kroenke, Spitzer, & Williams, 2001). The instrument was composed of ten items based on DSM-IV diagnostic criteria, each scored from 0 (*not at all*) to 3 (*nearly every day*) (Cronbach's α =. 91).

Patients' viral loads were self-reported. Participants were asked to report their viral loads based on their latest blood tests and whether they were currently taking ART therapy, which is in line with the self-reported viral load measure previously adopted by Halkitis et al. (2003).

4.7.4 Data analysis

Statistical analyses were conducted with SPSS 15.0 (Statistical Package for the Social Sciences; Chicago, IL) and Mplus 6.10 (Muthén & Muthén, 2010). Variable distributions were assessed through skewness and kurtosis (SPSS 15.0). Exploratory factor analyses (EFA) and structural equation modeling (SEM) were performed by

using Mplus 6.10. The WLSMV estimator was used because of the small sample sizes (Muthén & Muthén, 2010).

The number of factors to extract (EFA-promax rotation) was determined by considering three criteria: χ^2 and RMSEA values, which should be non-significant and lower than .06 (Steiger & Lind, 1980), and factor interpretability. The SEM goodness of fit indexes included the Tucker-Lewis incremental fit index (TLI; Tucker & Lewis, 1973), the comparative fit index (CFI) (Bentler, 1990), RMSEA, and the χ^2/df ratio (Crowley & Fan, 1997). CFI and TLI scores ≥ .95 indicated a good fit, whereas scores ≥ .90 indicated a sufficient fit. An RMSEA score lower than or equal to .05 indicated a good fit, whereas a score lower than or equal to .08 indicated a sufficient fit. A χ^2/df ratio lower than 5 indicated a good fit (Bollen, 1989; Crowley & Fan,1997; Hu & Bentler, 1999). Factor reliability was assessed with Cronbach's α.

4.7.5 Results

4.7.5.1 HIV-ASES exploratory factor analysis (EFA)

The variables violated the assumption of normal distribution and were therefore treated as ordinal. However, Mplus 6.10 does not allow ordinal variables to exceed ten categories, and since the HIV-ASES items contained eleven categories, we proceeded as follows: first, a non-parametric correlation matrix was calculated (Spearman's rho), and EFA was then performed on such a matrix. A three-factor solution resulted in a non-significant Chi-square test of model fit (p = .30), RMSEA = .031, and good factor interpretability. Notably, the second and third dimensions extracted corresponded to those extracted by Johnson et al. (2007) (see Table 1 for variables loading and factor reliability); the three factors extracted were labeled as follows (within the parentheses, the number of items is reported):

1. *Compliance self-efficacy* (six items): The items' content reflected the individuals' perceptions of being capable of following the therapeutic plan, a concept strictly related to compliance or to the "taking medications" behavior.
2. *Integration* (three items): the individuals' perceptions of being able to integrate HIV treatment into their daily lives.
3. *Perseverance* (three items): This factor exactly overlaps the one found by Johnson et al. (2007), and it refers to individuals' perceived ability to adhere to their treatment regimens, even during adversity.

4.7.6 HIV-ASES, depression, and viral load (SEM)

The factors extracted were significantly and highly inter-correlated (polychoric correlation coefficients were greater than .81 and were all significant at $p < .001$); thus, a second-order factor, namely ART adherence self-efficacy, was tested within structural equation modeling. This second-order factor was expected to be associated with lower levels of depression and a lower viral load. The model, reported in Figure 3, resulted in a good fit: $\chi^2/df = 1.76$, RMSEA = .08, and CFI/TLI = .96/.96, and the second-order factor, "HIV adherence self-efficacy" (the item loading on first-order factors ranged from .59 to .99), showed a significant association with depression (depression's item loadings ranged from .61 to .78) and viral load. Depression was not correlated with viral load.

Study 2

4.7.7 Method

The participants (N = 95) were women (30.53%) and men (69.47%) recruited at the Infectious Diseases Institute of Sant'Orsola Hospital (Bologna, Italy). Their mean age was 40.25 years (SD = 8.07).

A professional nurse in the Infectious Diseases Institute recruited participants and also cosigned and gathered the informed consent forms and self-report questionnaires. The recruitment of the patients occurred over seven months (from September 2010). The study was approved by the Research Ethics Committee of the Sant'Orsola Hospital (Bologna, Italy), and all patients enrolled signed written informed consent forms.

4.7.8 Measures

HIV adherence self-efficacy was assessed by using the Italian version of HIV-ASES (HIV Adherence Self-Efficacy Scale) (2007). The internal consistency was optimal (Cronbach's α = .92).

Depression was assessed through the PHQ-9 (Patient Health Questionnaire; Kroenke, Spitzer, & Williams, 2001), which also resulted in an optimal internal consistency (Cronbach's α =. 92).

Medication adherence was assessed through the Simplified Medication Adherence Questionnaire (SMAQ; Knobel, Alonso, Casado et al., 2002), a six-item questionnaire translated into Italian by the authors of this paper. Items 1, 2, 3, and 5 (sample item: "*Do you ever forget to take your medicine?*") were rated on a two-point scale: *Yes* (1)/*No* (2). Item 4 ("*Thinking about the last week, how often have you not taken*

your medicine?") was rated on a five-point answer scale from *Never* (1), *1/2 times* (2), *3/5 times* (3), *6/10 times* (4), to *10 times* (5). Item 6 ("*Over the past three months, on how many days have you not taken any medicine at all?*") was rated on a two-point scale: (1) < *2 days* and (2) > *2 days*. Items 4 and 6 were inverted; therefore, a higher SMAQ score corresponded with higher medication adherence (Cronbach's α =. 67). The viral loads at t0 (baseline) and t1 (after four months) were collected from the patients' clinical records.

4.7.9 Data analysis

Statistical analyses were conducted with SPSS 15.0 (Statistical Package for the Social Sciences; Chicago, IL) and Mplus 6.10 (Muthén & Muthén, 2010). Skewness and kurtosis were calculated in order to assess the variable distributions. With Mplus 6.10, structural equation modeling (SEM) was performed with WLSMV because of the non-normal distribution of the variables and the small size of the samples (Muthén & Muthén, 2010). Goodness of fit indexes included the Tucker-Lewis incremental fit index (TLI) (Tucker & Lewis, 1973), the comparative fit index (CFI) (Bentler, 1990), RMSEA, and the χ^2/df ratio (Crowley & Fan, 1997). CFI and TLI scores ≥ .95 indicated a good fit, whereas scores ≥ .90 indicated a sufficient fit. An RMSEA score lower than or equal to .05 indicated a good fit, whereas a score lower than or equal to .08 indicated a sufficient fit. A χ^2/df ratio lower than 5 indicated a good fit (Bollen, 1989; Crowley & Fan,1997; Hu & Bentler, 1999). Cronbach's α was calculated to assess the factors' reliability.

4.7.10 Results

4.7.10.1 HIV-ASES, depression, compliance, and viral load (SEM)

The HIV-ASES factorial model was tested on a SEM; additionally, the association of HIV adherence self-efficacy with depression and compliance was also tested. Lastly, HIV adherence self-efficacy and compliance's association with viral load (t0 and t1) was also tested. As shown in Figure 4, the model resulted in very good fitness indexes: $\chi^2/df = 1.17$, CFI/TLI = .98/.97, and RMSEA = .04. HIV-ASES (item loading on first-order factors ranged from .550 to .920), which resulted in a negative correlation with depression (item loading ranged from .712 to .913) and a positive correlation with compliance (item loading ranged from .526 to .910). Depression was associated with lower compliance, which, in turn, was inversely correlated with viral load. HIV-ASES and compliance predicted lower viral loads after a four-month follow-up.

4.7.11 Discussion

Adherence to HAART medications may be considered to be a key concept that plays an important role in patients' self-management of HIV infection. Indeed, they are actively involved in their therapeutic plans and consequently may participate in determining their clinical outcomes. Thus, being strictly adherent to medical prescriptions, both behavioral and pharmacological, may lead to a more favorable HIV progression biomarkers profile (e.g., an undetectable viral load). However, poor adherence levels may not ensure a slowdown in the progression of HIV, compromising patients' general health status. The reasons for poor adherence might be linked to psychological factors; therefore, individuals must perceive themselves to be fully capable of following the prescriptions and, therefore, of being adherent.

Namely, high HIV adherence self-efficacy may play a role in adherence and HIV self-management (Johnson et al., 2007). This construct is easily assessed through HIV-ASES (HIV - Adherence Self-Efficacy Scale), a self-report instrument developed by Johnson et al. (2007). To the best of our knowledge, no similar instruments are currently available in Italian. Thus, in this paper, we translated HIV-ASES into Italian, evaluating its dimensionality and psychometric properties on two separate samples of HIV-positive individuals. In contrast to the English version of HIV-ASES, which was composed of two dimensions, the Italian version's results were composed of three first-order factors underlying a second-order dimension labeled "HIV adherence self-efficacy." In line with Johnson et al. (2007), the first-order factors were labeled as follows: (1) compliance self-efficacy (an individual's perception of being able to stick to the treatment schedule), (2) integration (an individual's perception of being able to integrate HIV treatment into his or her daily life), and (3) perseverance (an individual's perception of being able to adhere to HAART treatment regimens, even when HIV-related adversities occur). The observed difference in the factorial model might be due to the difference between the psychometric approach used in this paper and the one adopted by Johnson et al. (2007), as well as to the difference in the sample sizes. Indeed, Johnson et al. (2007) used the ML estimator on the matrix of raw data, whereas in this work, the EFA was performed with WLSMV on a Spearman correlation matrix because the variables were non-normally distributed. Although raw data may be more informative than a correlation matrix, our results, which may still need to be replicated on a larger sample, may provide information on adherence self-efficacy. The accurate analysis of the dimensions' items suggests that our results may reflect a semantically-driven dimensionality. Indeed, the dimensions "compliance self-efficacy" and "integration" composed a unique dimension in Johnson and colleagues' work. We hypothesize this difference to

be a consequence of the effect of items wording. Namely, the items of the compliance self-efficacy dimension refer to the behavior of "taking medicine," whereas the integration items semantically refer to the integration of therapy into patients' lives. Lastly, it should be not denied that cultural differences, as well as the translation procedure, may also influence dimensionality, but this could be further investigated by conducting a cross-cultural study.

The factors extracted in this work could be considered to be the cardinal concepts of individuals' perceived self-efficacy with regards to being adherent to their HIV management regimens. More precisely, we refer to the concept of integration, which is related to patients' perceptions of being able to include medication and medical appointments in their daily routines. In addition, we also refer to perseverance, which represents the perception of the ability to persevere in taking medication, even when unexpected adversities occur. The "extra factor" represents one's perception of being capable of being compliant and taking medicine correctly and continuously. Since these factors were highly correlated, more so than Johnson et al. (2007) found, we hypothesized and confirmed that they were undergirding a second-order factor that we labeled "HIV adherence self-efficacy." This second-order factor was associated with lower levels of depression (Bandura, 1989) and an undetectable viral load (Johnson et al. 2007; Johnson, Sevelius, Dilworth, Saberi, & Neilands, 2012). The latter aspect is mediated by greater compliance, which, in turn, helps in maintaining an undetectable load and achieving better clinical outcomes. Moreover, when patients feel that they can successfully manage their HIV, depression may be less likely to occur, and we suggest that depression reflects a cognitive evaluation of one's condition. More precisely, in the presence of greater self-efficacy, HIV infection might be perceived as a less invalidating and more manageable condition. This result also

leads to a further consideration that is linked to depression as a predictor of poor compliance (Bhatia et al., 2011; Kroenke, Spitzer, & Williams, 2001; Halkitis et al., 2003).The effect of adherence self-efficacy on depression should be tested longitudinally, in order to confirm its action. Then, in the clinical context of HIV treatment, psycho-education intervention intended to increase self-efficacy might be conducted in order to increase patents' physical and mental well-beings. Our results may only confirm that baseline compliance and perceived self-efficacy independently predict undetectable viral loads after four months. This result confirms the central role of compliance and might also suggest that a different pathway, e.g., the neuroendocrine one (Cole, 2008), is involved in HIV progression, which could link perceived self-efficacy with lower viral loads. However, caution must be used in drawing this conclusion because this may only reflect a measurement artifact caused by the psychometric assessment. However, in order to verify this hypothesis, we have recently concluded a longitudinal study in which pro-inflammatory cytokines and salivary cortisol, both involved in the neuroendocrine pathway, have also been assessed, along with perceived self-efficacy.

In conclusion, our preliminary data, as well as Johnson et al.'s (2007; Johnson et al., 2012) work, provide information on eligible psycho-educational interventions in an HIV context, confirming HIV-ASES's reliability and predictive properties. Therefore, we suggest that in their clinical practices, clinicians may use this instrument in individuating patients who are at risk of poor compliance. Additionally, we cautiously suggest that HIV adherence self-efficacy could be the target of psycho-educational interventions in the context of HIV clinics because of its positive effects on mental and physical health. The cross-sectional nature of the studies might limit our conclusions on mental health; in fact, the directionality of the association between

HIV-ASES and depression might not be clear. However, we are currently conducting a longitudinal study in order to clarify this. In addition, self-reported measures (e.g., viral load) could also represent a limitation, although only if the Study 2 viral load were not self-reported. Lastly, the convenience sampling method and relatively modest sample sizes may also limit the generalizability of the results. We would encourage researchers to overcome such limitations by providing more robust results, which might help in the development of effective psycho-educational interventions.

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Table 1 HIV-ASES EFA. Three-factor model loading and factor reliability (Cronbach's alpha)

		1	2	3
		α=.88	**α=.89**	**α=.78**
4	Stick to your treatment schedule even when your daily routine is disrupted?	.90	-.14	.08
3	Integrate your treatment into your daily routine even if it means taking medication or doing other things in front of people who don't know you are HIV-infected?	.58	.21	-.13
7	Continue with your treatment even if doing so interferes with your daily activities?	.49	.12	.22
6	Stick to your treatment schedule when it means changing your eating habits?	.46	.14	.15
5	Stick to your treatment schedule when you aren't feeling well?	.45	.04	.28
1	Stick to your treatment plan even when side effects begin to interfere with daily activities?	.42	.12	.22
2	Integrate your treatment into your daily routine?	.26	.68	-.11
11	Continue with your treatment even when people close to you tell you that they don't think that it is doing any good?	-.08	.66	.31
10	Continue with your treatment even when getting to your clinic appointments is a major hassle?	.02	.51	.24
12	Get something positive out of your participation in treatment, even if the medication you are taking does not improve your health?	.04	-.03	.82
9	Continue with your treatment even when you are feeling discouraged about your health?	.02	.23	.66
8	Continue with the treatment plan your physician prescribed even if your T-cells drop significantly in the next three months?	.09	-.00	.61

Figure 1 Theoretical model of the HIV-ASES factorial structure and its expected association with, depression, and viral load (Study 1)

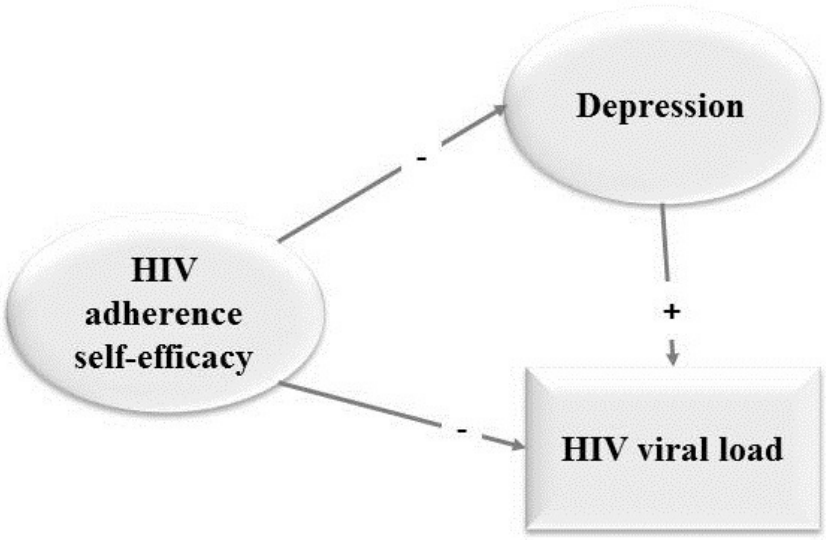


Figure 2 Theoretical model of the factorial structure of HIV-ASES and its expected association with depression, compliance, and viral load measured on two times (Study 2)

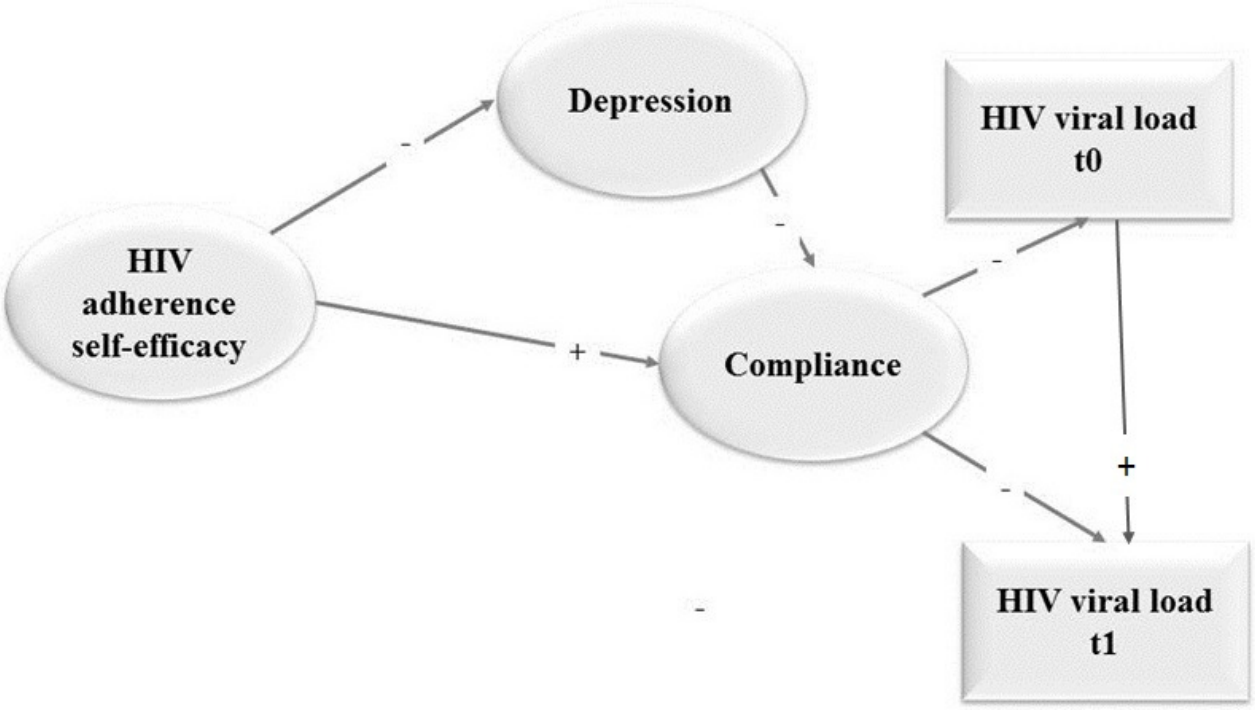
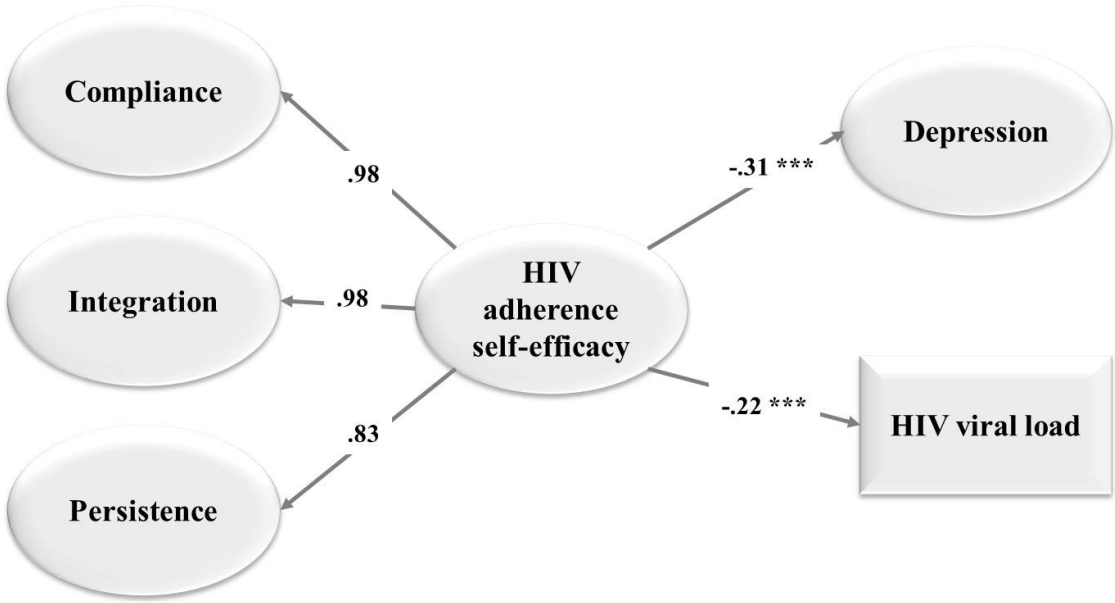


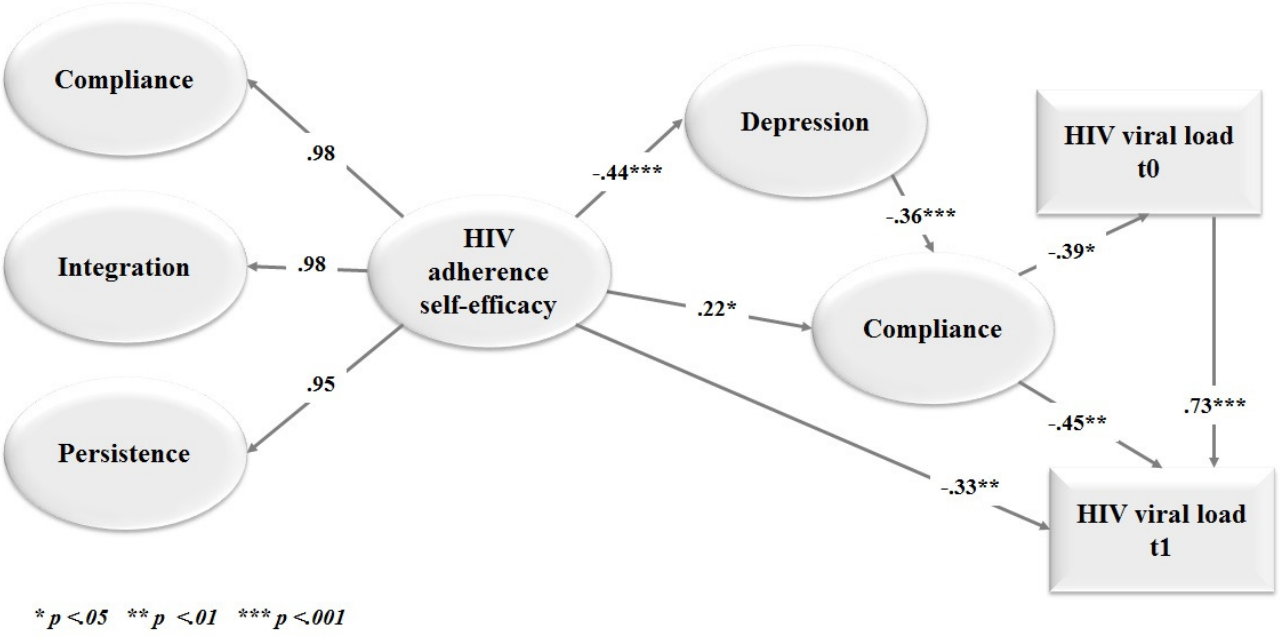
Figure 3 Second order factor model of HIV-ASES and its significant association with depression, and viral load (SEM – Study 1)



*** $p < .001$

Ellipses within the figure indicate latent variables; rectangle represents the self-reported observed variable.

Figure 4 Second order factor structure of HIV-ASES and its significant association with depression, compliance, and viral load at t0 and t1 (SEM – Study 2)



Ellipses within the figure indicate latent variables; rectangles represent observed variable. Viral load measures were referred to baseline (t0) and 4 months follow-up (t1).

4.8 Building a bridge to connect the physiological and psychological factors linked to HIV infection

Norcini Pala, A., & Steca, P.

Abstract

HIV infection is linked to well-being through, at least, physiological and psychological pathways; in fact, because of HIV-related inflammation, the risk of depression may be magnified. Furthermore, there are psychological factors that could influence HIV progression negatively, e.g., by amplifying the inflammatory response. For instance, perceived stress is thought to play an important role as it is connected with cortisol and cytokines production as well as with depression. However, several psychological aspects (e.g., personality, emotions, and social support) can buffer the negative effect of stress. With this work we aimed at evaluating whether cytokine dysregulation and cortisol were associated with HIV progression biomarkers, over time (two time-points), and testing whether such physiological dysregulation corresponded to greater depression. Furthermore, we were interested in testing perceived stress correlation with cytokines and cortisol, and in conclusion, we evaluated the effect of personality typologies, emotions, and social support on stress, hypothesizing them to exert a positive effect on well-being (e.g., reducing stress and depression) over time. The personality typologies tested have been previously identified by us in a previous study, and resulted differently characterized with emotions and depression. Ninety patients recruited at S. Orsola hospital (Bologna, It) have been followed over time (eight months) and accordingly evaluated; they compiled a battery of questionnaires and provided a sample of saliva to assess cortisol. The results indicated that the inflammation generated by HIV-1 infection remained quite stable over 8 months; the increase in perceived stress corresponded with greater depression, whereas increased viral load (over time) was associated with greater TNF-α, which was highly correlated with lower CD4+ cells count. Interestingly, we found that increased levels of IL-6 were associated with higher depression. No associations were found among viral load and monocytes count, or between the latter and the cytokines. However, the

personality prototypes resulted differently linked to depression levels over time, and with emotions; furthermore, greater perception of spouse social support corresponded to lower level of stress. Therefore, despite the confirmed greater inflammation observed in HIV-positive individuals and its relationship with depression, there may be peculiar aspects of personality and romantic/social relationship that might prevent the development of depression.

Key words: Perceived stress; Cytokines; Cortisol; HIV-1; Depression

4.8.1 Introduction

HIV infection is a delicate and complex chronic illness that despite the great innovations in the treatments that substantially enhanced patients' quality and length of life remains a partially unexplored disease. In fact, there is a constellation of factors associated with HIV infection that still must be understood and that go from the physiological aspects to the social factors undoubtedly passing across the psychological ones. Therefore, the approach to HIV infection should be multidisciplinary accounting for the connection between the immune system and psychological functioning, which has been confirmed by several studies (e.g., Dantzer, 2012; Raison, Capuron, & Miller, 2006) and could be mediated by the hypothalamic-pituitary-adrenal (HPA), and the nervous system (SN) (Zunszain, Anacker, Cattaneo, Carvalho, & Pariante, 2011). This connection, however, may be rather complicate and intricate (Dantzer, 2012), although HIV virus and more precisely the TAT protein, have been proven experimentally to promote the production of pro-inflammatory cytokines such as TNF-α in the brain (Fu, Lawson, Kelley, & Dantzer, 2011). Likewise, Temoshok and colleagues (2009) found that the psychological constructs of alexithymia and type c coping are differently associated with specific aspects related to HIV, namely chemokines and cytokines. In fact, one of the most ascertained aspects of HIV infection regards the cytokines dysregulation associated, which actually are produced in response to infection and may promote virus replication as well (Poli et al., 1990; Poli & Fauci, 1992; Poli et al., 1990). This dysregulation is mediated by monocytes (Kasang et al., 2012) and can be harmful for physical and mental health since cytokines could promote depression (Baraldi, Hepgul, Mondelli, & Pariante, 2012; Lawson, Kelley, & Dantzer, 2011) and virus replication (Poli et al., 1990), and their production could be increased by psychological stress (Fumaz et al., 2012). Hence, there is a physiological mechanism

through which HIV may act on mental health; furthermore, this connection is influenced itself by the psychological stress effects on immune system (Dickerson, Gable, Irwin, Aziz, & Kemeny, 2009; Dickerson, Gruenewald, & Kemeny, 2004). In fact, psychological stress could promote cortisol production (Gruenewald, Kemeny, & Aziz, 2006; Gruenewald, Kemeny, Aziz, & Fahey, 2004), which in its turn might reduce the immune system functioning (e.g., Campisi, Bravo, Cole, & Gobeil, 2012). Then, there is a sort of circularity in the relationships among psychological and physiological aspects lined to HIV infection. For this reason, we were interested in testing whether HIV positive individuals were characterized with greater pro-inflammatory cytokines and immune activation (e.g., monocytes) and if this was linked to immune system impairment. Besides, for the clinical relevance of TNF-α and Il-6, we were interested in understanding whether perceived stress corresponded to elevated levels of these cytokines, and if this was linked to greater risk of depression.

4.8.2 The person-center approach to explain individual difference: The personality prototypes

Although immune activation leads to a greater risk of depression, it is not negligible that individuals may have resources that protect them against the risk of mental disorders. At least two factors can be cited for their well-known beneficial effect that exert on well-being, namely personality and social support. The first is more "intra-individual", as it is firstly connected to the individuals' organization of personality traits in a unique and stable configuration; social support, which can actually be predicted by the personality (e.g., extraversion), is more inter-individual as it involves the social world of oneself.

To overcome the limits of a variable-centered approach that focuses on the linear relationship of individual variables with an outcome, we rather chose to adopt a person-centered approach in which typologies of individuals are identified based on psychosocial characteristics in order to account for the complexity of human being and the related phenomena. In fact, prototypes of personality based on the five traits of the Big Five model have been found (McCrae & Costa, 1997, 1999), and their relevance can be linked to the fact that such dimensions have been significantly related to mental health and well-being (Friedman, Kern, & Reynolds, 2010; Hampson & Friedman, 2008; Kern & Friedman, 2011). These prototypes have been called "overcontrolled," "undercontrolled," and "resilient" and consist, from the first through the last, in dysfunctional aspects (e.g., negative emotions) or/and functional aspects (e.g., positive emotions) (Berry, Elliott, & Rivera, 2007; Steca, Alessandri, & Caprara, 2010; Steca, Alessandri, Vecchio, & Caprara, 2007). Overcontrolled, for instance, are at greater risk of depression respect to the other two clusters (Berry et al., 2007; Norcini Pala & Steca, unpublished manuscript), whereas resilient are more prone to experience positive emotions, and to have more satisfying social relationships (Steca et al., 2010). The prototype of undercontrolled have been characterized with mixed characteristics, yet they may be less prone to develop depression (Berry et al., 2007). Hence, for the greater risk of depression in HIV positive individuals, we tested whether these prototypes were differently associated with depression, as we previously found in healthy individuals.

4.8.3 Social support and depression

Social support is connected to the natural tendency of human beings to have social relationships; family, friends, and the romantic partner are examples of the sources

of support that have demonstrated to limit the effect of stress (Cohen & Wills, 1985; Deno et al., 2012; Field & Schuldberg, 2011; Smith & Wang, 2012). In particular, there is evidence of a unique effect of the spouse support (Meuwly et al., 2012) in line with the hypothesis that the lack of support provided by a romantic partner cannot be compensated by the support from friends or family (Holt-Lunstad, Birmingham, & Jones, 2008). In fact, for instance, loneliness, which is a major issue for HIV-positive individuals (Grov, Golub, Parsons, Brennan, & Karpiak, 2010), is associated with greater use of antidepressants (Pulkki-Raback et al., 2012) and then, it may cause greater depression. Thus, this work was carried out also to verify if social support provided by romantic partner could attenuate perceived stress and reduce depression in a population that is at greater risk for depression (e.g., Rabkin, 2008).

4.8.4 Stress and cortisol: The mediation of emotions

There is wide consensus about the effect of emotions on stress. For instance, certain individuals may be more resistant to stress also for the effect of positive emotions (Tugade & Fredrickson, 2004; cf. Steca et al., 2010 and Folkman & Moskowitz, 2000b). Cotrairwise, emotional distress is associated with greater reactivity to stress and cortisol production (Campbell & Ehlert, 2012; Dickerson et al., 2009; Dickerson, Gruenewald, et al., 2004; Dickerson & Kemeny, 2004; Dickerson, Kemeny, Aziz, Kim, & Fahey, 2004). Therefore, we hypothesized that the individuals who tend to experience greater positive emotions, and less negative emotions, might be characterized with lower perceived stress.

4.8.5 Aims

This study aims at integrating three intricate levels on which HIV can be investigated, the physiological, the psychological, and psychosocial. From the inner physiological aspect of HIV infection we proposed to investigate whether HIV-1 (viral load) was associated with immune activation, conceived here as greater monocyte counts and pro-inflammatory cytokines (TNF-α, and Il-6). We focused on these two cytokines as they have demonstrated to be strictly involved in mental disorders (Corona et al., 2012; Dantzer, 2012) and HIV progression (e.g., Poli et al., 1990). Furthermore, in line with the literature (Steensberg, Fischer, Keller, Møller, & Pedersen, 2003) we tested the relationship among TNF-α and Il-6 with patients' salivary cortisol; perceived stress, in its turn, was expected to be related to greater TNF-α and Il-6, and cortisol (e.g., Kennedy, Kiecolt-Glaser, & Glaser, 1988). Then, we also wanted to verify whether depression was really correlated with pro-inflammatory cytokines (Fu et al., 2011) and monocytes, which are thought to promote pro-inflammatory cytokines production (cf. Kasang et al., 2012). Respect to the typologies of individual personality, we adopted a "classification" based on our previous study, where we found three profiles of individuals two of which overlap those found in previous work (e.g., Steca et al. 2010), whereas the third profile differed from that described in the literature, and we then decided to label "emotionally stable" individuals in this cluster. In fact, we found that the dimensions that characterized such a profile were those that compose the super factors described by DeYoung (2006) namely *stability* and lower *plasticity* which is the second super-factor described in the literature (DeYoung, Peterson, & Higgins, 2002). Resilient were characterized with higher stability and plasticity, whereas overcontrolled individuals were characterized with greater plasticity and lower stability (cf. Norcini Pala & Steca, unpublished manuscript; see also Berry et al., 2007). Stability has been linked to serotonergic

system, therefore, in line with our study we hypothesized overcontrolled to be at greater risk of depression. Accordingly, we have also hypothesized that the resilient individuals who demonstrated to have more satisfying social relationships, might benefit of partner social support much more than overcontrolled. Furthermore, in line with Dickerson and Kemeny (2004) and Folkman and Moskowitz (2000a, 2000b), we hypothesize that those individuals characterized with greater positive emotions should be less affected by stress.

4.8.6 Method

4.8.6.1 Participants and procedure

Ninety patients followed by the infectious diseases department of S. Orsola Hospital (Bologna, Italy) have been recruited; they were men (65%) and women (25%) with a mean age of 38.43 (*SD* = 8.14) years, and with a range of age from 21 to 57 years. The majority of them was gay (56.67%; men), less than a half heterosexuals (36.66%; 10% men and 26.67 women) and 6.67% bisexuals (men). Patients were preponderantly on ART 72.91%, whereas naïve to ART were 27.09%. Most of them reported to be currently engaged in a romantic relationship (60.22%), whereas less than a half were single (39.78%). Participants' education background included elementary (1.14%) and junior high school (27.27%), the majority possessed high school diploma (46.59%), university degree (6.82%), master's degree (9.09%), and Ph.D. or other specialization (9.09%).

Participants were randomly recruited (starting from May 2011) from a list of scheduled medical appointment and screening; in fact, HIV-positive patients followed at S. Orsola Hospital (Bologna, Italy) generally schedule three blood screenings and clinical visits per year, and we had access to the monthly visits

scheduled from May to October 2011. We excluded patients younger than 18 years because the parents' informed consents should have been provided; we excluded co-infected patients (with any viral illness such as hepatitis) since they might have been characterized with a more complex physiological and psychological condition, and non-Italian speakers in order to avoid language biases. For each day of the scheduled plan (composed of an average of 20 patients per day), we randomly selected five patients using an algorithm of SPSS. The selected participants were contacted telephonically, and of the 109 who agreed with participation 19 (17.43%) dropped-out eventually; in fact, they received the battery of questionnaires but never compiled nor submitted to us. Participants were informed that the participation was voluntary and that all the information provided would not have been disclosed nor their identities revealed; in fact, the data were analyzed in aggregate form. All participants received, read, signed the informed consent on the day of their blood test, and were informed that we would have collected the biomarkers about their clinical condition by consulting their clinical records directly. This study was approved by the S. Orsola Malpighi Ethical Committee.

4.8.7 Measures and Instruments

4.8.7.1 *Clinical indicators*

HIV-progression biomarkers were viral load and CD4+ cells count, and were both assessed on the day that patients received the battery of questionnaires. CD4+ cells counts are expressed in percentage, namely the percentage of the T-cells CD4+ within the total population of the leucocytes; at baseline, percentages ranged from 6% to 52% with a mean of 29.16% (SD = 9.48), after 8 months, the range was 3% to 52% and the mean was 29.62 (SD = 9.59). Viral load was expressed as copies (of virus) per

ml of blood, it ranges from non-detectable, namely under the threshold of the detectability of laboratory instruments (generally < 50 copies/ml but it may vary) to 380000 copies/ml (mean 17031 and SD = 49704.22); after 8 months, the laboratory that conducted the analysis changed their laboratory instruments and were able to provide a more accurate detection of viral load, specifically < 20 copies / ml or even *not-traceable*. However, in order to compare the two time-points, we recoded the values under 50 copies / ml, as undetectable. The maximum value observed was 70127 copies/ml and the mean was 9399.73 copies / ml (SD = 18686.44).

Cytokines were assessed by the central laboratory of the hospital; TNF-α (*immunoenzymatic methods*) was expressed in pg/L; Il-6 (chemiluminescence method) was expressed in pg/mL; monocytes were expressed in percentage of cells. Salivary cortisol was determined through ELISA kits (Pantec s.r.l. Turin, Italy) used to analyze the samples of saliva (for each time-point) gathered just after the awakening time on the day patients' blood screening. They were instructed to produce a sample before they brushed their teeth and before they had breakfast, the saliva samples were collected in urine containers. Our intent was to investigate the association of psychological constructs with cortisol production soon after waking (within 15 minutes of waking). However, we are aware that cortisol may significantly vary during the day (or even within the first hour of awaking time); in fact, our intent was not to assess daily cortisol production dysregulation (or AUC area under the curve). Furthermore, when patients are asked to produce multiples saliva samples during a whole day, patients' adherence would be drastically impaired, especially if it is seen as a difficult practice. These biomarkers were collected at each of the two time-points.

Viral load at both time-points, cortisol of first time-point, Il-6 and TNF-α of both time-points violated the normal distribution assumption thus, according to Barbaranelli (2006), we used the linear transformations to correct the departure. Viral load was transformed in its logarithm-10 that corrected departure from normality, after the transformation kurtosis and skewness were lower than 1.0. TNF-α, at each time-point was corrected through the logarithm 10, since SQRT did not work, after the transformations, kurtosis and skewness were both lower than .72. Il-6 consistently departed from the normal distribution, the linear transformation that worked on the variables was the transformation in its reciprocal, kurtosis and skewness were now lower than .70 except for kurtosis of t_0 Il-6 that resulted =1.0 but still lower than before (2.78). Monocytes and CD4+ cells counts (%), instead, were normally distributed.

4.1.9.2 Psychological assessment

Perceived Stress was assessed two times (baseline and after 8 months) with the Recent (over the last 4 weeks) Perceived Stress Questionnaire (Levenstein et al., 1993) that assesses 7 stress-related dimensions (harassment, overload, irritability, lack of joy, fatigue, worries, tension) through 30 items rated on a 4-point scale ranging from 1 (*Almost never*) to 4 (*Usually*). The literature about the instrument showed that perceived stress assessed with this instrument resulted associated with ulcerative colitis activity, depression, and perceived stress scale by Cohen et al. (Cohen, Kamarck, & Mermelstein, 1983) cf. Levenstein et al. (1993). The Cronbach's alpha was greater than .93 at each time-point.

Personality traits were assessed (at baseline) with the short form of the Big Five Questionnaire (BFQ; Caprara, Barbaranelli, Borgogni, & Perugini, 1993), composed

of 60 items relative to the 5 traits and their 10 facets, each of them assessed with 6 items scored on a 5-point scale: from complete disagreement (1 = *Very false for me*) to complete agreement (5 = *Very true for me*). The five dimensions assessed were Energy (E) that refers to Extraversion (McCrae & Costa, 1986), organized into two facets: "Dynamism" (expansiveness and enthusiasm), and "Dominance" (assertiveness and confidence). Besides, Openness (O) was organized into the two facets of "Openness to Culture" (essentially referred to the broadness or narrowness of one's own cultural interests) and "Openness to Experiences" (e.g., openness to novelty, interest toward different people, habits and life-styles); whereas, Agreeableness (A), was organized into the facets "Cooperativeness/Empathy", (concern and sensitiveness towards others and their needs) and "Politeness", (kindness, civility, docility and trust). Emotional Stability (ES) was related to Neuroticism (N) and consists in the two facets of "Emotion Control" (the capacity to cope adequately with one's emotionality) and "Impulse Control" (the capability of controlling irritation, discontent, and anger). Conscientiousness (C), instead, is organized into two facets, "Scrupulousness" (e.g., orderliness and precision) and "Perseverance" (the capability of fulfilling one's own tasks and commitments; Caprara et al., 1993). The variables were all normally distributed, therefore we computed the Cronbach's alpha of the five domains that ranged from .61 to .89, indicating sufficient reliability.

Depression was assessed two times (baseline and after 8 months) with the Patient Health Questionnaire (PHQ-9; Kroenke, Spitzer, & Williams, 2001) a widely and reliable instrument that consists of 9 items referred to the diagnostic criteria of depression of which participants frequency from 0 (*Not at all*) to 3 (*Nearly every day*) during prior 2 weeks. An extra item, excluded by the overall score assesses if the

symptoms rated influenced patients' lives. According to Kroenke et al. (2001), indeed, an overall score of depression was obtained calculating the sum of the first nine items. Cronbach's alpha indicated very good reliability of the scale (α = .84 and at t_1 α = .83).

Partner social support was assessed through three items, on which participants rated to what extent their partner supported them with respect their illness providing 1) emotional support, 2) informative support, or 3) instrumental. The items were rated on a five-point scale that ranged from 0 "not at all" to 5 "very much". The Cronbach's alpha was .87, and at t_1 .92.

Emotions were assessed with the Derogatis Affects Balance Scale (DABS; Derogatis & Rutigliano, 1996), an instrument that we translate in Italian language and that consisted in 40 adjectives that describe "How people feel". Twenty items refer to positive emotions and twenty to negative emotions. The instrument is particularly versatile and can be used to assess discrete emotions, positive and negative emotions, as well as indexes such as emotional balance (Positive/Negative). We decided to use the overall score of the two dimensions, negative and positive, and tested them by calculating Cronbach's alpha which resulted greater than .91 for negative emotions and .94 for positive emotions. Since we were interested in testing positive emotions, we calculated, in line with Derogatis & Rutigliano (1996) an overall score of positive emotions resulted by the formula = Positive emotions - Negative emotions.

4.8.8 Data analysis

SPSS 20 (Statistical Package for the Social Sciences, Chicago, IL) and AMOS 16 were used to perform the analyses; skewness and kurtosis were computed to assess variables distribution and factors reliability was assessed with Cronbach's alpha (SPSS 20). Variables that departed from the normal distribution were linearly transformed; we firstly tested square root, if it did not work in reducing normality violation we then attempted the logarithmic transformation and the reciprocal eventually. These transformations have been computed for viral load, Il-6, cortisol, TNF-α, because the path-analysis, which is based on multiple regression analysis, requires the normal distribution of variables (Barbaranelli, 2006).

To reproduce the same clusters as those we formed in our previous work, we used the discriminant scores obtained on such study and on the basis of the scores obtained in the present work on the Big Five. The formula used was $(X^1*ES) + (X^2*C) + (X^3*O) + (X^4*A) + (X^5*E) + (K)$ and substantially replicate the discriminant function found in our previous study. The X^n within the formula are the Big Five dimensions' discriminant score on each of the clusters we found in our previous study. For each cluster, and we have three clusters to form, the Big Five dimensions showed peculiar discriminant score, which multiplied for the Big Five *actual* score (namely that of the participants of the present work) provide 3 overall scores (3 classes). Then through a conditional statement (e.g., if class1 < class2 and class3 > class2 then membership is cluster 3; cf. Nie, Hull, Jenkins, Steinbrenner, & Bent, 1975) three clusters were formed, and labeled "Overcontrolled", "Emotionally stable", and "Resilient".

Two path-analyses were conducted to investigate the reciprocal relationship of clinical biomarkers over time (after 8 months), and to verify whether the changes in perceived stress, depression, were associated and mediated by changes in cytokines

and cortisol. Besides, within the same analysis we also tested personality profiles, positive emotions and spouse social support in relation with perceived stress.
The goodness-of-fit indexes were the Tucker-Lewis Incremental fit index (TLI; Tucker & Lewis, 1973), the Comparative Fit Index (CFI; Bentler, 1990), RMSEA, and the χ^2/df ratio (Crowley & Fan, 1997). CFI and TLI scores ≥ .95 indicated good fit, while scores ≥ .90 indicated sufficient fit. A RMSEA score ≤.05 indicated a good fit, whereas a score ≤ .08 indicated a sufficient fit of the model. A χ^2/df ratio ≤5 indicated a good fit for the model (Bentler, 1990; Bollen, 1989; Crowley & Fan, 1997; Hu & Bentler, 1999; Schermelleh-Engel, Moosbrugger, & Muller, 2003).

4.8.9 Results

4.8.9.1 *HIV biomarkers, cytokines, and cortisol*

On the first part of the study, we wanted to explore the correlations between the physiological parameters related to HIV infection, to have an overall pictures of the pattern underlying the illness. In table 1 we reported the correlations and flagged the significant ones. At time t_0 viral load correlated with lower CD4+ (%), with greater TNF-α, Il-6 and cortisol; TNF-α was linked to greater cortisol, greater Il-6, and lower CD4+ (%). Cortisol and Il-6 as well showed an inverse relationship with CD4+ (%). The results of the analysis of the data at t_1 partially replicated those at t_0, in fact, viral load still resulted highly correlated with lower CD4+ (%) and TNF-α, which was correlated with Il-6 and lower CD4+ (%). The correlations between the two time-points were significant as well; in fact, viral load at t_0 correlated with viral load at t_1, as well as with lower CD4+ (%) and increased TNF-α, and slightly significantly with Il-6. TNF-α at t_0 correlated with viral load at t_1, Il-6, TNF-α (t1) and with lower CD4+ (%). The latter was correlated with the CD4+ (%) after 8 months. It clearly appeared that over the two time points, there was continuity, and that to greater viral load

corresponded greater inflammation as well as lower CD4+ cells count. In addition, we wanted to verify whether monocytes, which are thought to be activated by HIV-1 virus and to mediate the production of cytokines, resulted coherently correlated with the biomarkers discussed above. Table 2 reports the results of the analysis showing, indeed, that monocytes were significantly, and coherently, associated with viral load and TNF-α and inversely with CD4+ cells count. Monocytes at t_0 and t_1 were highly correlated over the time point ($r = .68$, $p < .001$), and there is support about a general activation of the immune system over time and monocytes are involved in this activation.

4.8.10 *Relationship between clinical biomarkers over the two time points*

The results obtained have been graphically reported in figure 1; the biomarkers essentially resulted highly associated after 8 months, except for the relation between TNF-α and Il-6 and TNF-α and cortisol that resulted significant only at t0, and viral load on monocytes that was significant at t1, and the association were around the same magnitude. Notably, TNF-α at t0 predicted Il-6 at t0 and t1, whereas the autoregression of Il-6 t0 on t1, did not result significant.

4.8.11 Perceived stress, depression and their relationship with spouse social support, personality profiles, and positive emotions

As a first step we tested whether the constructs assessed were related over time, thus we performed a path-analysis that resulted with good fit ($\chi^2/df = 1.89$, CFI/TLI = .97 / .94, RMSEA < .07; fig. 2); it clearly emerged that those who were depressed at t_0 showed greater depression at t1 as well, and so resulted individuals who scored higher on depression. The positive effect of spouse support was barely significant ($p <$

.05) and only at t_0, greater stress resulted in greater depression at both time-points, there was an association between the personality prototype and the positive emotions which showed to mediate the relationship between personality prototype, and depression ($\beta = -.34$, $p < .01$) and stress ($\beta = -.32$, $p < .01$) at t_0 and depression ($\beta = -.25$, $p < .01$) and stress ($\beta = -.39$, $p < .01$) at t_1 . Positive emotions assessed at t_0 resulted indirectly associated with lower stress ($\beta = -.63$, $p < .001$) and lower depression ($\beta = -.52$, $p < .001$) at t_1. Suggesting that stress and depression may be persistent over time, and that positive emotions may represent an important resource to cope with stress.

4.8.12 *The relationship between psychological factors and the changes in clinical biomarkers*

With a path-analysis we tested the correlations among the changes (calculated as the difference of each variable: t_1-t_0) in depression, perceived stress, spouse support, and the clinical biomarkers. To assess these changes we calculated the mathematical difference among t1 and t0 for each of them; therefore, these new variables must be interpreted, as follows: greater positive value "the level was increased from t0 to t1" passing through the null changes, which meant "no changes over time", and higher negative value, referred to reduced levels over time. Positive emotions and personality profiles were assessed only at t0. The path-analysis resulted with a good fit ($\chi^2/df = 1.09$, CFI/TLI = .96 / .94, RMSEA < .05); the results have been reported in figure 3, and the non-significant associations were excluded to improve the readability of the graph.

A change in stress resulted in greater depression; stress resulted lowered if participants have perceived greater support by their spouses over time. Interestingly, the changes in CD4+ (%) were predicted by the changes in TNF-α but not by viral load, which still resulted highly correlated with TNF-α. The association between personality profile and positive emotions could confirm that resilient individuals could be characterized with greater positive emotions. The personality prototypes were associated with Il-6 changes and more precisely, Il-6 increase over time resulted slightly lower in resilient individuals than in emotionally stable and overcontrolled. Interestingly, we found that a increased Il-6 corresponded to greater level of depression.

4.8.13 Discussion

The aim of this work was to investigate the relevant aspects linked to HIV infection, at several levels, from the physiological, to the psychological until the psychosocial (social support), bridging them into a possible connection based on the literature produced so far.

The main results of this work are that the infection and the viral load in HIV positive individuals produce immune activation, consisting in greater monocytes, and inflammatory cytokines that may trigger further chain reactions. In fact, TNF-α and Il-6 might play a fundamental role in HIV progression (Poli et al., 1990) and both are produced by monocytes in response to HIV infection. However, despite the correlations initially observed, monocytes tested within path-analyses were not associated the cytokines. Our results support the studies that showed the replication of virus to be accompanied by greater monocytes, and most likely by macrophages (Bennasser, Badou, Tkaczuk, & Bahraoui, 2002) and lower CD4+ (%).

The perception of stress may be extremely influent on mental health as demonstrated by our results, in fact after eight months individuals might persist in their condition and may also show stable levels of depression. As suggested by Rabkin (2008) although subclinical, depression in HIV-positive patients may be extremely resistant and should be properly addressed with medications or psychotherapy. Positive emotions and personality prototype could represent positive resources that help individuals to cope with stress; greater positive emotions (Steca et al., 2010) and lower risk of depression might characterize individuals with resilient and those with the "emotionally stable" profile.

Cortisol was expected to impair immune system functioning (Dhabhar, 2009), however it did not emerge from our results and it was not correlated with perceived stress; likewise, we expected to find greater TNF-α and Il-6 in those individuals with greater perceived stress, but we did not confirm this hypothesis.

Another important aspect is related to HIV-positive individuals' characteristics and dynamic; indeed, perceived stress may be responsible of depression, or co-responsible, and might predict depression, or non-remission, after 8 months. Individuals who were characterized with the "resilient" personality profile tended to experience greater positive emotions and also showed lower Il-6 over the time. This may mean that the protective role of this profile might be due to physiological changes. However, these results may worth to be investigated more adequately. Partners' social support resulted protective against stress, that resulted reduced when the perception of social support increased, in line with the literature, then, (Holt-Lunstad et al., 2008) the support provided by intimate partner may have a strong effect contrasting the percpetion of stress (cf. Norcini Pala & Steca, unpublished manuscript). In conclusion, for the effect of perceived stress on mental health and

possibly on physical health, such construct deserves great attention and might be included in the clinical practice. Depression was confirmed as great issues that may afflict HIV-positive individuals and may persist after months. Based on the results of this study, however, we found that there are persons who are more capable to resist especially when they benefit from the support of a romantic partner. Il-6 has demonstrated to be correlated with higher depression at follow up after 8 months; more generally greater deregulation in the immune system has been observed, therefore the interplay of cytokines in promoting depression may be more complex than in HIV-negative persons.

Table 1 HIV progression biomarkers, cytokines and cortisol t_0 and t_1 - Pearson's r correlation

		1	2	3	4	5	6	7	8	9
1	**Viral Load (t0)**	**1.00**								
2	**Cortisol (t0)**	**.22***	**1.00**							
3	**Il-6 (t0)**	**.24****	**.12**	**1.00**						
4	**TNF-α (t0)**	**.45*****	**.31****	**.36*****	**1.00**					
5	**CD4+ % (t0)**	**-.37*****	**-.25****	**-.21***	**-.45*****	**1.00**				
6	**Viral Load (t1)**	.72***	.01	.01	.39***	-.12	**1.00**			
7	**Cortisol (t1)**	-.011	.23*	.03	-.04	-.02	**-.01**	**1.00**		
8	**Il-6 (t1)**	.20*	-.03	.12	.22**	-.02	**.04**	**-.06**	**1.00**	
9	**TNF-α (t1)**	.39***	.01	.10	.46***	-.12	**.73*****	**-.00**	**.24****	**1.00**
10	**CD4+ % (t1)**	-.37***	-.23*	-.06	-.25***	.72***	**-.34*****	**-.09**	**-.08**	**-.44*****

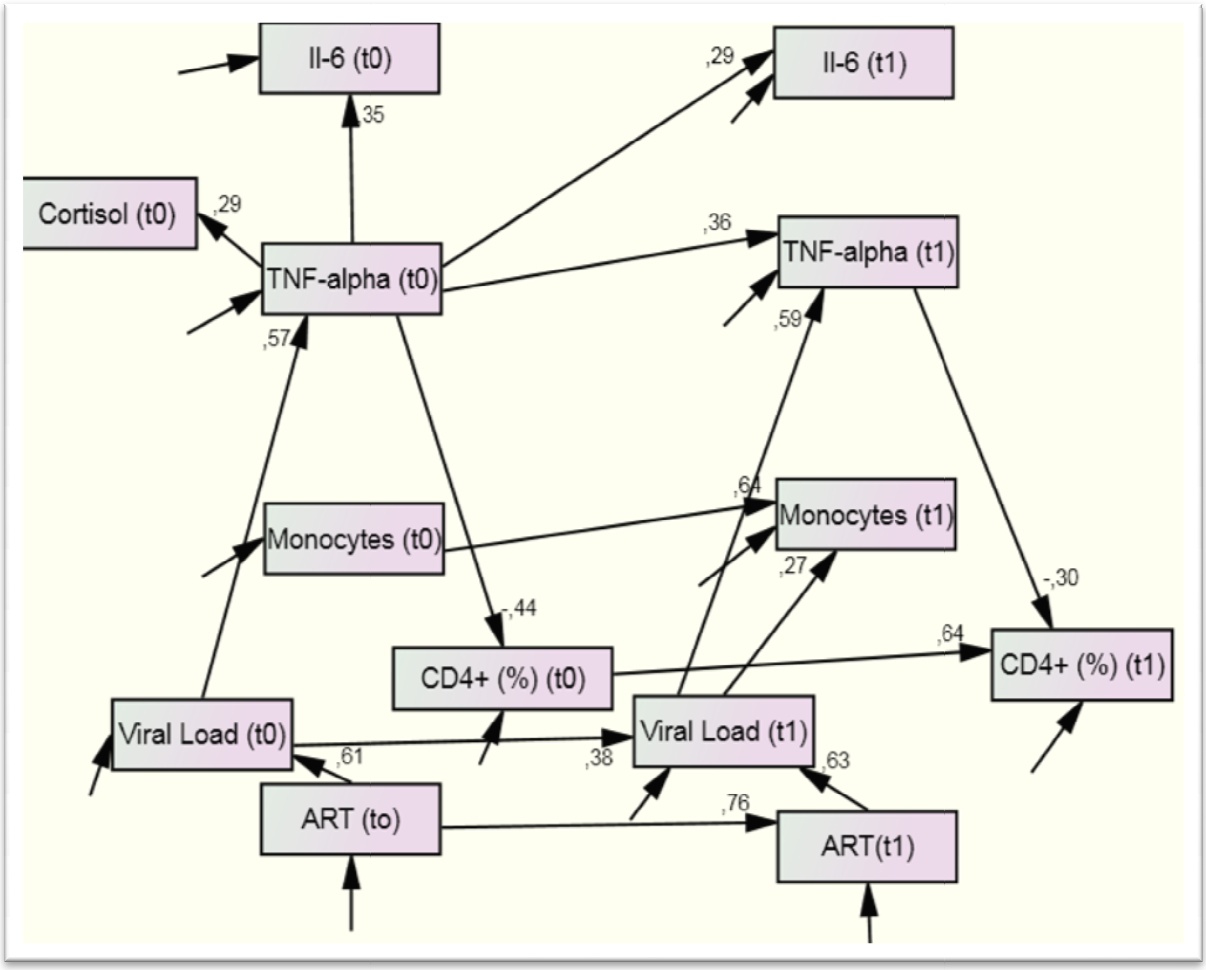
** p < .05, ** p <.01, *** p < .001*

Table 2 Monocytes' (to and t1) correlations with HIV-biomarkers and cytokines.

	Monocytes (t0)	Monocytes (t1)
Viral load (t_0)	**.21***	.29**
Il-6 (t_0)	**.07**	.06
TNF-α (t_0)	**.21***	.08
CD4+ (%) (t_0)	**-.31****	-.31**
Viral load (t_1)	.31*	**.43****
Il-6 (t_1)	-.00	**-.06**
TNF-α (t_1)	.28*	**.35****
CD4+ (%) (t_1)	-.22	**-30****

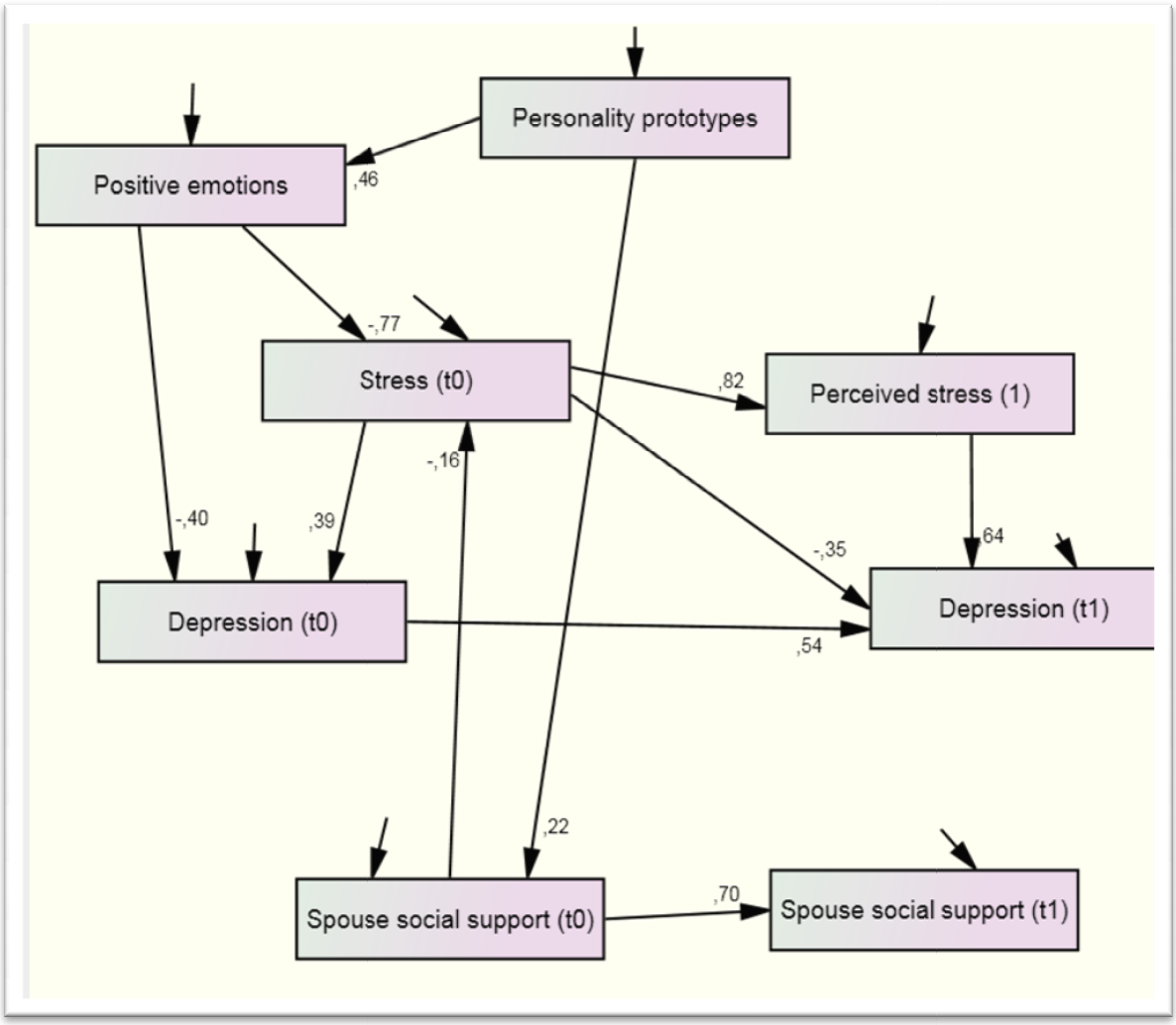
*$p < .05$, **$p < .01$

Figure 8 Clinical biomarkers' relationships over the two time points - Path-analysis



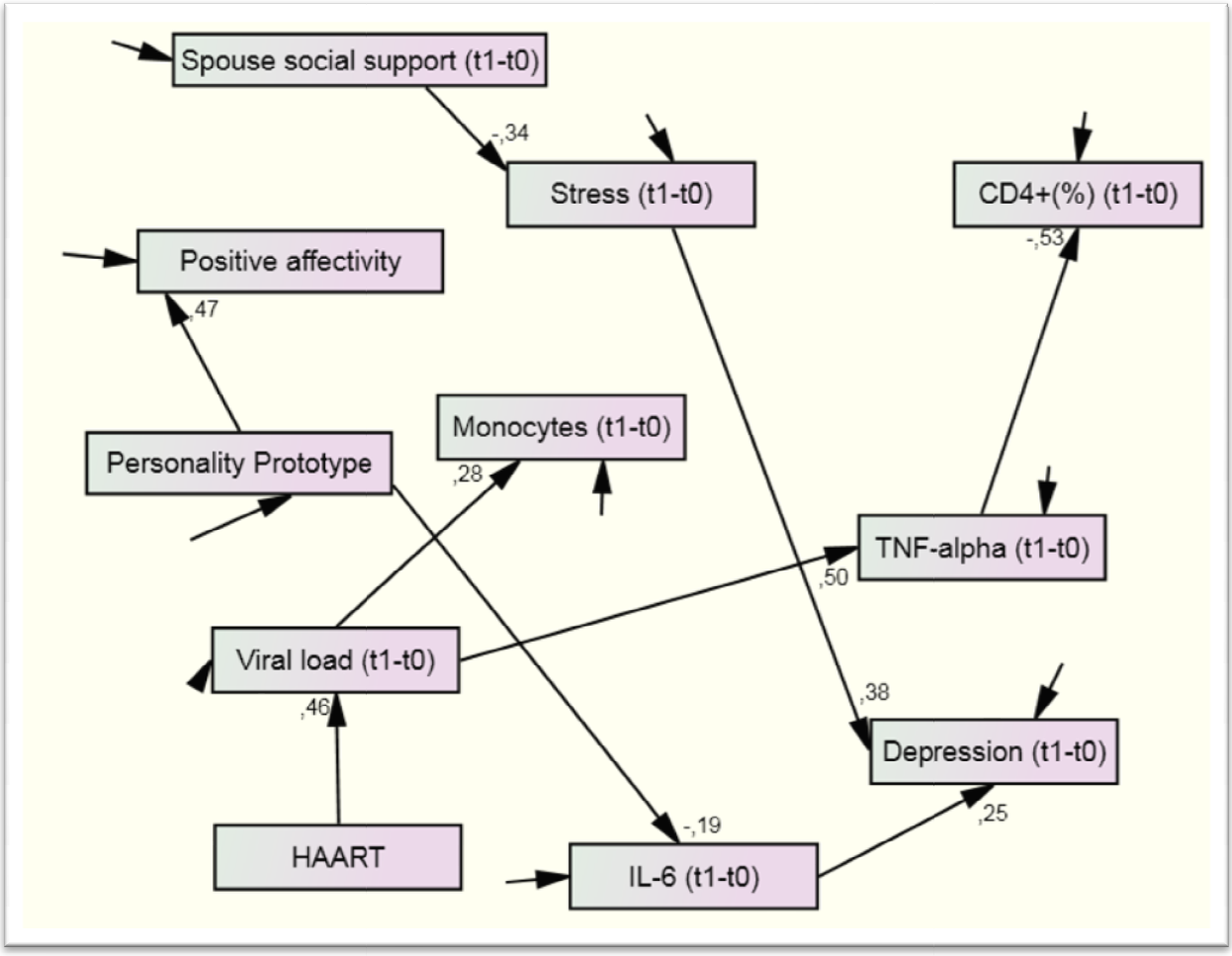
All the relationships reported within the figure were significant at least with p < .05

Figure 9 Perceived stress, depression and spouse social support and their relationships with personality prototypes and positive emotions.



All the relationships reported within the figure were significant at least with p < .05

Figure 3 Inter-relationships of the clinical biomarkers' variations over time (t1-t0) and their association with the personality prototypes, perceived stress, spouse social support, and positive affectivity



All the relationships reported within the figure were significant at least with $p < .05$

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4.9 General Discussion and Conclusion

The objective of this work was to investigate the psychosocial factors related to HIV infection that, on the basis of scientific literature produced so far, have demonstrated to be extremely important in the clinical setting. In this chapter, we have illustrated the results of our studies that we conducted according to the literature presented in the early chapters of this work. One of the most relevant construct that proven to be dangerously associated with mental and physical health is perceived stress (Fumaz et al., 2012; Martínez-Sánchez & Ato, 2011; Schlotz, Hammerfald, Ehlert, & Gaab, 2011; Temoshok, Garzino-Demo, Smith, & Wiley, 2011) and all the related constructs such as emotions, coping (Folkman, 2008; Folkman & Moskowitz, 2000a, 2000b), and personality (Penley & Tomaka, 2002). The studies presented in this chapter confirmed the centrality of perceived stress and may suggest that the other psychological constructs such as alexithymia and the perception of social stigma may be influential (Schwartz & Meyer, 2010). Furthermore, several aspects may also act unconsciously, such as internalized homophobia or implicit emotions, without increasing stress perception but still promoting cortisol production (e.g., Quirin, Kazén, Rohrmann, & Kuhl, 2009). Nonetheless, we also individuated psychosocial aspects that could play a protective effect; in fact, partner social support, personality, and coping strategies may all mediate and moderate the stressfulness of adverse events linked to HIV. More precisely, following the person-centered approach that aims at individuating profiles of individuals and specifically the peculiar organization of individuals' characteristics, we found that, as regards their personality, there are patients that could be at greater risk to develop depression but some that may benefit from social support more than other, as for resilient persons (cf. Steca et al., 2010). Furthermore, there are specific features that could exert a protective role by moderating the effect of stress on the physiological reaction. Overall, we found that

among the three personality profiles identified (overcontrolled, emotionally stable and resilient), the buffering effect of partner social support may be efficacious only for resilient people, whereas in those who are "overcontrolled", one may conduct stress management intervention, since the relationships of perceive stress and depression over time seemed to be more consistent than in resilient individuals. Furthermore, as observed in the study about adherence self-efficacy, individuals who perceive to be capable to deal with ART therapy compliance could show lower perceived stress and depressive symptoms (Johnson et al., 2006; Johnson et al., 2007), therefore psycho-educative intervention aimed at improving self-efficacy beliefs might be feasible in HIV-care contexts. However, we believe that our results should be investigated on larger samples and possibly on several time-points, in order to determine a reliable trend and directionality of influence.

Undoubtedly, we observed that the perception of control and to possess the necessary skills to cope with difficult situations related to HIV (coping) are extremely important; in fact those who perceive lower control over their condition might eventually engage in dysfunctional coping such as alcohol use or show poorest well-being (Broadbent, Ellis, Thomas, Gamble, & Petrie, 2009a, 2009b; Chen, Tsai, & Chou, 2011; Petrie, Perry, Broadbent, & Weinman, 2011). Moreover, we would encourage the use of psychometric instruments to assess depression such as PHQ-9 (Kroenke, Spitzer, & Williams, 2001), which could be easily administered and interpreted by physicians that follow HIV-positive individuals. Firstly, because on the basis of our results, the rates of depression in people with HIV may be higher and more severe than in the general population; furthermore, because after 8 months, depression did not improved (see our last contribution) and, in line with the literature (Rabkin, 2008), we can hypothesize that even if subclinical, depression

may persist if not properly treated. Moreover, improvement in depressive symptoms showed significant improvement in adherence to ART (Dalessandro et al., 2007; Walkup, Wei, Sambamoorthi, & Crystal, 2008).

There is no doubt that HIV-positive patients may show peculiar pattern of inflammatory response (Fu, Lawson, Kelley, & Dantzer, 2011; Lawson, Kelley, & Dantzer, 2011; Li, Yim, & Lau, 2010; Segerstrom & Kemeny, 2006) but it could be hardly compared to that of different populations. Therefore, although it has been commonly assumed that TNF-α and IL-6 could cause depression in HIV-positive patients (Fu et al., 2011) one may also assume that for the cytokines dysregulation, the relationship between inflammation and depression could be more complex than simply linear. Lastly, we strongly believe that psychological profiles that are based, e.g., on personality, on illness perceptions, or on individuals' resources such as coping and positive emotions, may help to identify patients that are at risk for depression, stress, dysfunctional behaviors, and may help to identify the aspects that exert a protective effect on mental and physical health.

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