ΟΛΙΣΤΙΚΗ ΔΙΑΧΕΙΡΙΣΗ ΑΣΘΕΝΟΥΣ ΜΕ ΨΩΡΙΑΣΙΚΗ ΝΟΣΟ
Η ΟΠΤΙΚΗ ΤΟΥ ΨΥΧΙΑΤΡΟΥ

Δημήτρης Ρούκας
Ψυχίατρος
Κέρκυρα, 19 Απριλίου 2019

ΔΗΛΩΣΗ ΣΥΓΚΡΟΥΣΗΣ ΣΥΜΦΕΡΟΝΤΩΝ

ΤΑΚΤΙΚΕΣ ΑΠΟΔΟΧΕΣ: Ιδιωτικό Ιατρείο (Αθήνα), Υ.ΕΘ.Α

ΟΜΙΛΙΕΣ: Servier, Specifar, Brain Therapeutics, Lundbeck, Innovis, Novartis

ΜΕΛΕΤΕΣ: Lundbeck, Servier, ELPEN

ΕΚΠΑΙΔΕΥΣΗ: Servier, Specifar, Lundbeck, Innovis, ELPEN

Διευκρινίσεις...

- Η παρουσίαση αυτή προορίζεται μόνο για μη-προωθητικό επιστημονικό σκοπό και μπορεί να περιέχει πληροφορίες σχετικά με τα προϊόντα ή τις ενδείξεις τους, που επί του παρόντος μπορεί να είναι υπό διερεύνηση ή/και που δεν έχουν εγκριθεί από τις ρυθμιστικές αρχές.

- Η παρουσίαση αυτή εκφράζει αποκλειστικά τις απόψεις του ομιλητή.

- Οι πληροφορίες που περιέχονται είναι ακριβείς κατά τη δημιουργία της παρουσίασης.

- Τυχόν δεδομένα σχετικά με προϊόντα τα οποία δεν ανήκουν στη Novartis βασίζονται σε δημόσια διαθέσιμες πληροφορίες κατά τη δημιουργία της παρουσίασης.

Περίγραμμα παρουσίασης…

- Ψωρίαση
- Ψυχοκοινωνικές επιπτώσεις στους ασθενείς με ψωρίαση
- Παθοφυσιολογικοί μηχανισμοί ψωριασικής νόσου
- Παθοφυσιολογικοί μηχανισμοί κατάθλιψης
- Συνύπαρξη ψωριασικής νόσου και κατάθλιψης
- Κατάθλιψη (επιδημιολογία, διάγνωση, κλινική εικόνα)
- Συμπεράσματα

Ψωρίαση…

- Η ψωρίαση είναι μια κοινή, μη μεταδοτική, αυτοάνοση νόσος που επηρεάζει μέχρι και το **3%** του παγκόσμιου πληθυσμού
- 125.000.000 πάσχουν από ψωρίαση παγκοσμίως,
- 15.000.000 πάσχουν από ψωρίαση στην Ευρώπη και
- **250.000** πάσχουν από ψωρίαση στην **Ελλάδα**
- η ψωρίαση επηρεάζει την εργασία και την παραγωγικότητα
- οι ασθενείς με ψωρίαση λαμβάνουν κατά μέσο όρο:

26 μέρες αναρρωτικής άδειας το χρόνο

European Academy of Dermatology and Venereology (EADV) Congress 2016. September 28 – October 2; Vienna, Austria.

The Clear about Psoriasis survey is the largest global survey to date of people with moderate-to-severe psoriasis. It includes 8,338 participants across 31 countries and was supported by 25 patient groups from around the world.[1]

*Countries include: Argentina, Australia, Austria, Belgium, Brazil, Bulgaria, Canada, Czech Republic, Denmark, Finland, France, Germany, Hungary, India, Ireland, Israel, Italy, Japan, Mexico, Netherlands, Norway, Portugal, Romania, Russia, S. Korea, Sweden, Switzerland, Taiwan, Turkey, UK and USA

June 2016

Skin to live in

#Ask4Clear
skintolivein.com/ask4clear

European Academy of Dermatology and Venereology (EADV) Congress 2016. September 28 – October 2; Vienna, Austria.

The Clear about Psoriasis survey

the Psoriasis Area Severity Index (PASI), Sleep Scale MOS, WHO-5 Quality of Life and Stanford Presenteeism Scale. Moderate-to-severe psoriasis was defined as patients either having a PASI score of 10 or above, or alternatively they had a PASI score between 5 and 9.9, with psoriasis plaques on either their face, palms, hands, fingers, genitals, soles of feet and/or nails.

Who took part?

GENDER

55%

Mean age **43**

45%

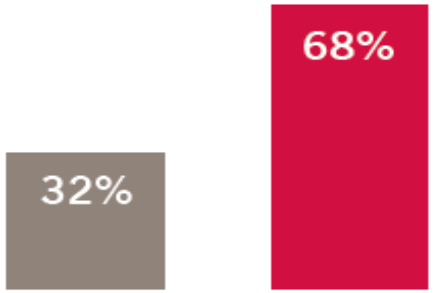
Mean age **45**

PASI

The average PASI score of participants:

14.3

PASI SPLIT



June 2016

Skin to live in

#Ask4Clear

skintolivein.com/ask4clear

European Academy of Dermatology and Venereology (EADV) Congress 2016. September 28 – October 2; Vienna, Austria.

The Clear about Psoriasis survey

Humiliation and Discrimination

45% have been asked if they are contagious

84%

of people with psoriasis suffer discrimination or humiliation

34% have been stared at in a swimming pool

16% of people with psoriasis have been refused service in a beauticians, hairdressers, barbers or shop

June 2016

Skin to live in

#Ask4Clear

skintolivein.com/ask4clear

European Academy of Dermatology and Venereology (EADV) Congress 2016. September 28 – October 2; Vienna, Austria.

The Clear about Psoriasis survey

Treatment goals and expectations

On average, **people see three different medical professionals and try four different treatments** before getting a treatment that works

Only 45% of people with psoriasis feel clear or almost clear skin is an achievable goal

28% took more than five years to get a treatment that gave them clear or almost clear skin

23% of people with psoriasis are still managed by their GP instead of a dermatology specialist

June 2016

Skin to live in

#Ask4Clear

skintolivein.com/ask4clear

European Academy of Dermatology and Venereology (EADV) Congress 2016. September 28 – October 2; Vienna, Austria.

The Clear about Psoriasis survey

Relationships

43%

of the total sample feels psoriasis has affected their relationships and of these...

15% have had a partner end a relationship with them because of their psoriasis

33% feel inadequate as a spouse or partner

50% avoid having sex or intimate relationships

27% cannot bear the thought of someone touching their skin

June 2016

Skin to live in

#Ask4Clear

skintolivein.com/ask4clear

European Academy of Dermatology and Venereology (EADV) Congress 2016. September 28 – October 2; Vienna, Austria.

The Clear about Psoriasis survey

Working lives blighted by psoriasis

54% of the total sample feels psoriasis has affected their work life and of these...

18% worry they will lose their job

14% are given tasks which limit their interaction with others

23% are made fun of by people in their working environments

38% do not feel fully productive because they itch so much

June 2016

Skin to live in

#Ask4Clear

skintolivein.com/ask4clear

European Academy of Dermatology and Venereology (EADV) Congress 2016. September 28 – October 2; Vienna, Austria.

The Clear about Psoriasis survey

Mental Health

38%

of people with psoriasis have been diagnosed with a psychological condition as a result of their psoriasis

25% have been diagnosed with anxiety and 24% with depression

16%

hide themselves away from the world

June 2016

Skin to live in

#Ask4Clear

skintolivein.com/ask4clear

- **Σύμφωνα με τα αποτελέσματα της έρευνας...**

European Academy of Dermatology and Venereology (EADV) Congress 2016. September 28 – October 2; Vienna, Austria.

- το 84% των ατόμων που ζουν με μέτρια ως σοβαρή ψωρίαση υφίστανται διακρίσεις και περιφρόνηση,
- το 34% δηλώνει ότι αισθάνεται να τους κοιτούν επίμονα όταν βρίσκονται σε δημόσιους χώρους (πισίνα),
- 55% των συμμετεχόντων δηλώνουν ότι έχουν πολύ χαμηλές προσδοκίες από τη θεραπεία τους, σε σχέση με την επίτευξη καθαρού δέρματος,
- 45% από τους ασθενείς με ψωρίαση είχαν ερωτηθεί αν το νόσημα τους είναι μεταδοτικό,
- το 16% των συμμετεχόντων παραδέχεται ότι επιλέγει την απομόνωση από το κοινωνικό σύνολο ως μηχανισμό αντιμετώπισης,
- το 24% των ασθενών πάσχει από κατάθλιψη...

- **Σύμφωνα με τα αποτελέσματα της έρευνας…**

European Academy of Dermatology and Venereology (EADV) Congress 2016. September 28 – October 2; Vienna, Austria.

- το 84% των ατόμων που ζουν με μέτρια ως σοβαρή ψωρίαση υφίστανται διακρίσεις και περιφρόνηση,
- το 34% δηλώνει ότι αισθάνεται να τους κοιτούν επίμονα όταν βρίσκονται σε δημόσιους χώρους (πισίνα),
- 55% των συμμετεχόντων δηλώνουν ότι έχουν πολύ χαμηλές προσδοκίες από τη θεραπεία τους, σε σχέση με την επίτευξη καθαρού δέρματος,
- 45% από τους ασθενείς με ψωρίαση είχαν ερωτηθεί αν το νόσημα τους είναι μεταδοτικό,
- το 16% των συμμετεχόντων παραδέχεται ότι επιλέγει την απομόνωση από το κοινωνικό σύνολο ως μηχανισμό αντιμετώπισης,
- **το 24% των ασθενών πάσχει από κατάθλιψη…**

Symptoms of Anxiety and Depression Among Adults with Arthritis — United States, 2015–2017

FIGURE 1. Age-standardized percentage* of adults reporting symptoms of anxiety and depression,† by arthritis§ status — National Health Interview Survey, 2015–2017

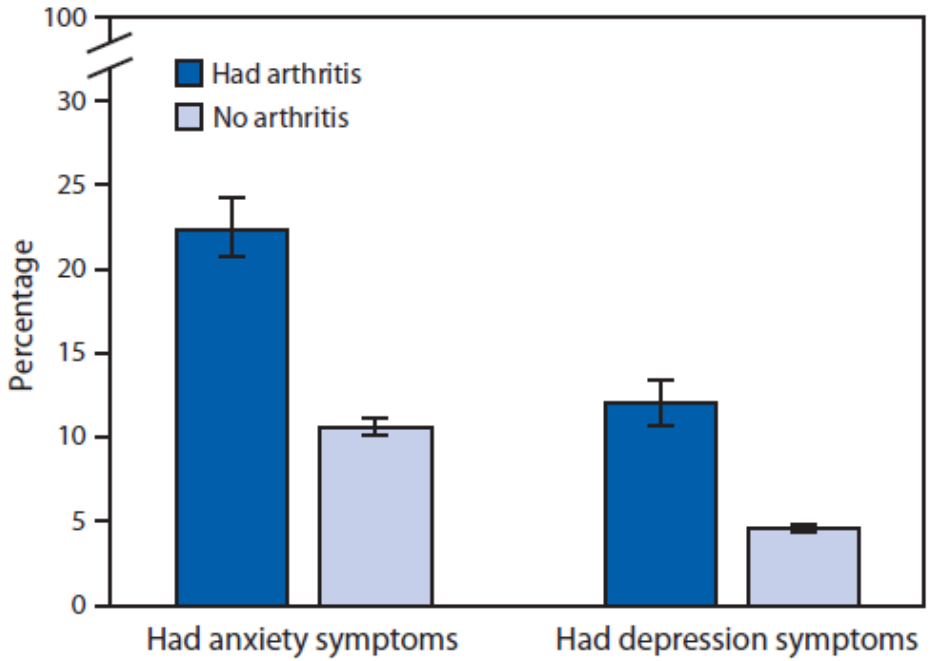
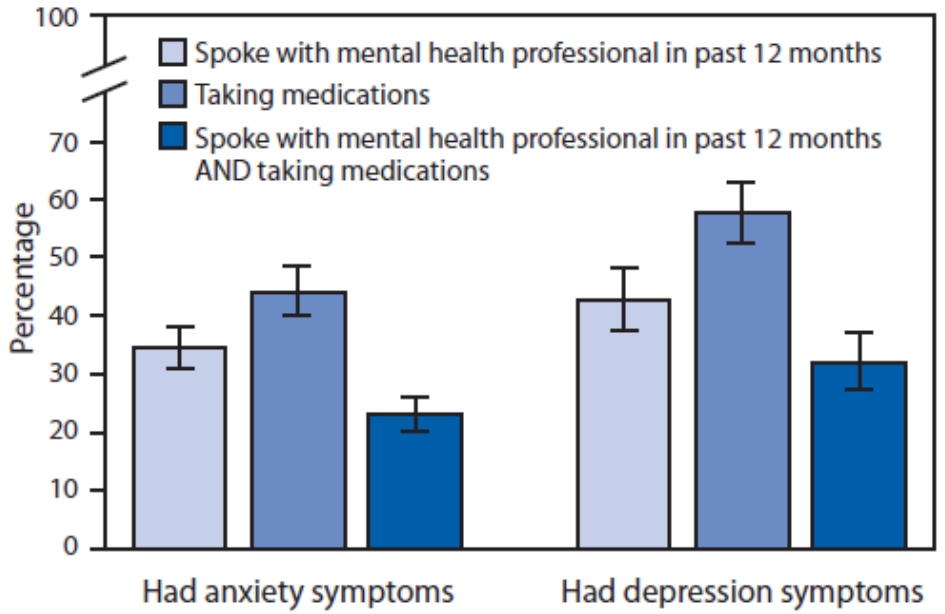


FIGURE 2. Age-standardized percentage* of adults with arthritis† reporting treatment for anxiety symptoms or depression symptoms,§ by type of treatment¶,** — National Health Interview Survey, 2015–2017



Managing Patients with Psoriatic Disease: The Diagnosis and Pharmacologic Treatment of Psoriatic Arthritis in Patients with Psoriasis

REVIEW ARTICLE

Drugs (2014) 74:423–441
DOI 10.1007/s40265-014-0191-y

Philip J. Mease · April W. Armstrong

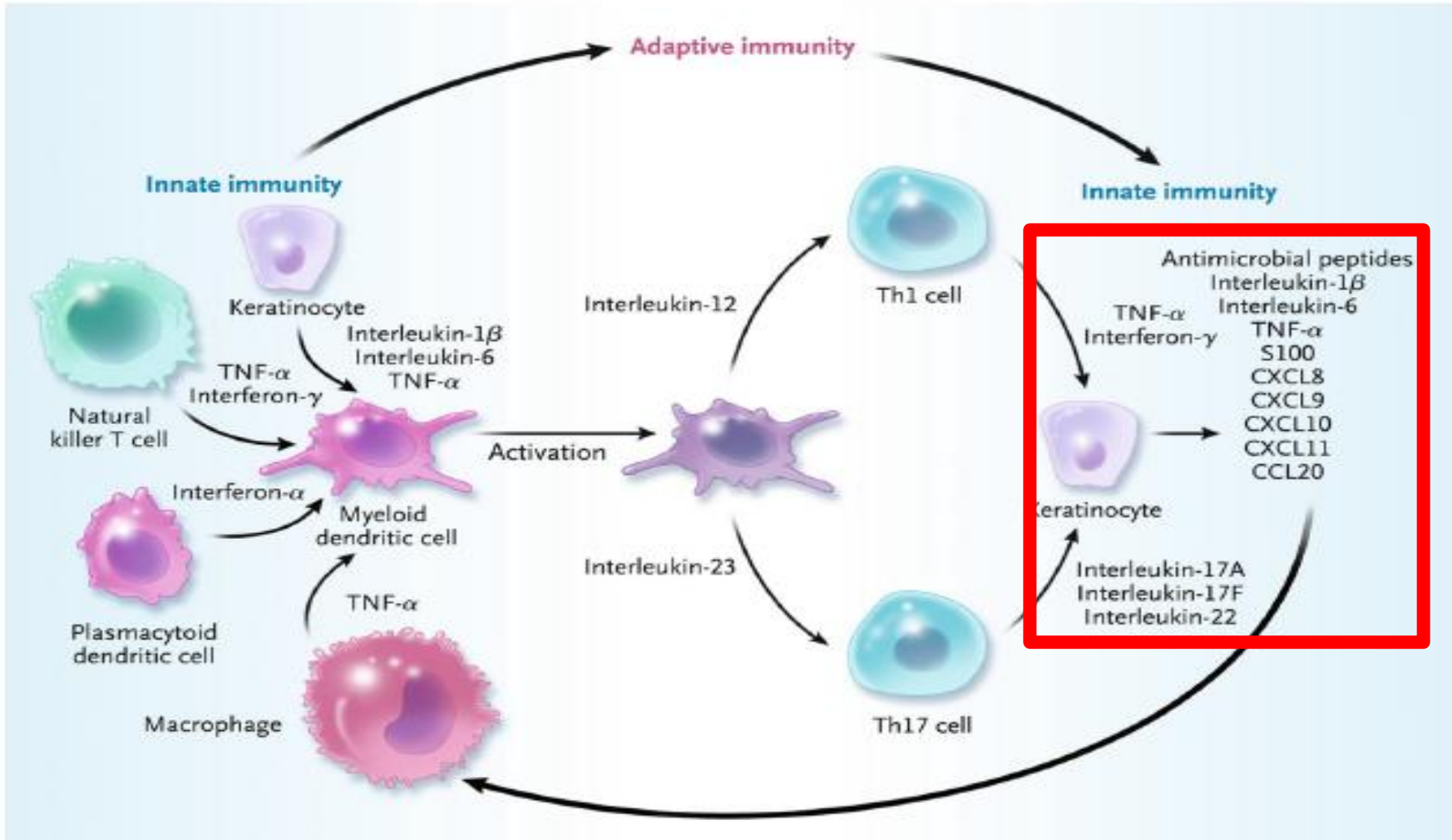


Fig. 2 Mechanisms of systemic, chronic inflammation in psoriasis and psoriatic arthritis. From Nestle et al. [1]. Copyright © 2009, Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society. *CCL* chemokine (C-C motif) ligand, *CXCL* chemokine (C-X-C motif) ligand, *Th* T helper, *TNF* tumour necrosis factor

Inflammation: A Contributor to Depressive Comorbidity in Inflammatory Skin Disease

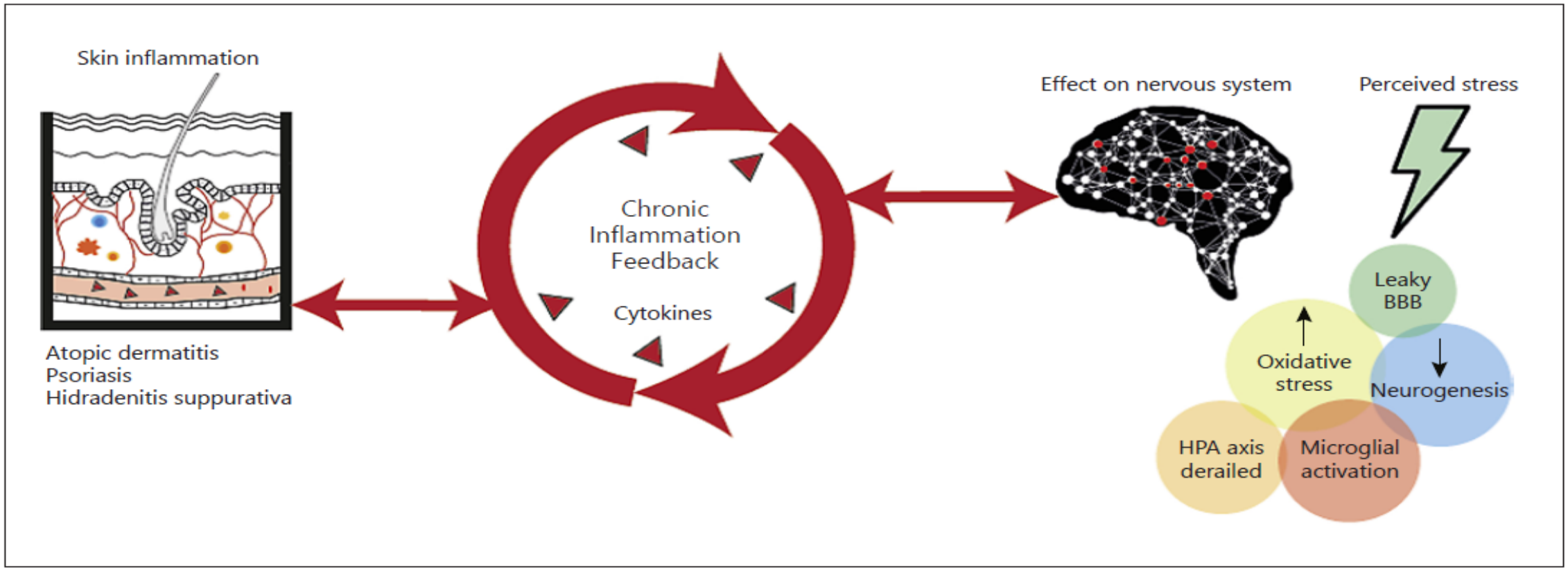


Fig. 1. The potential relationships between cutaneous inflammation and central nervous system contributions form a chronic feedback loop.

Skin Pharmacol Physiol 2018;31:246–251
DOI: 10.1159/000490002

Farzanfar/Dowlati/French/Lowes/Alavi

Παθοφυσιολογία της κατάθλιψης…

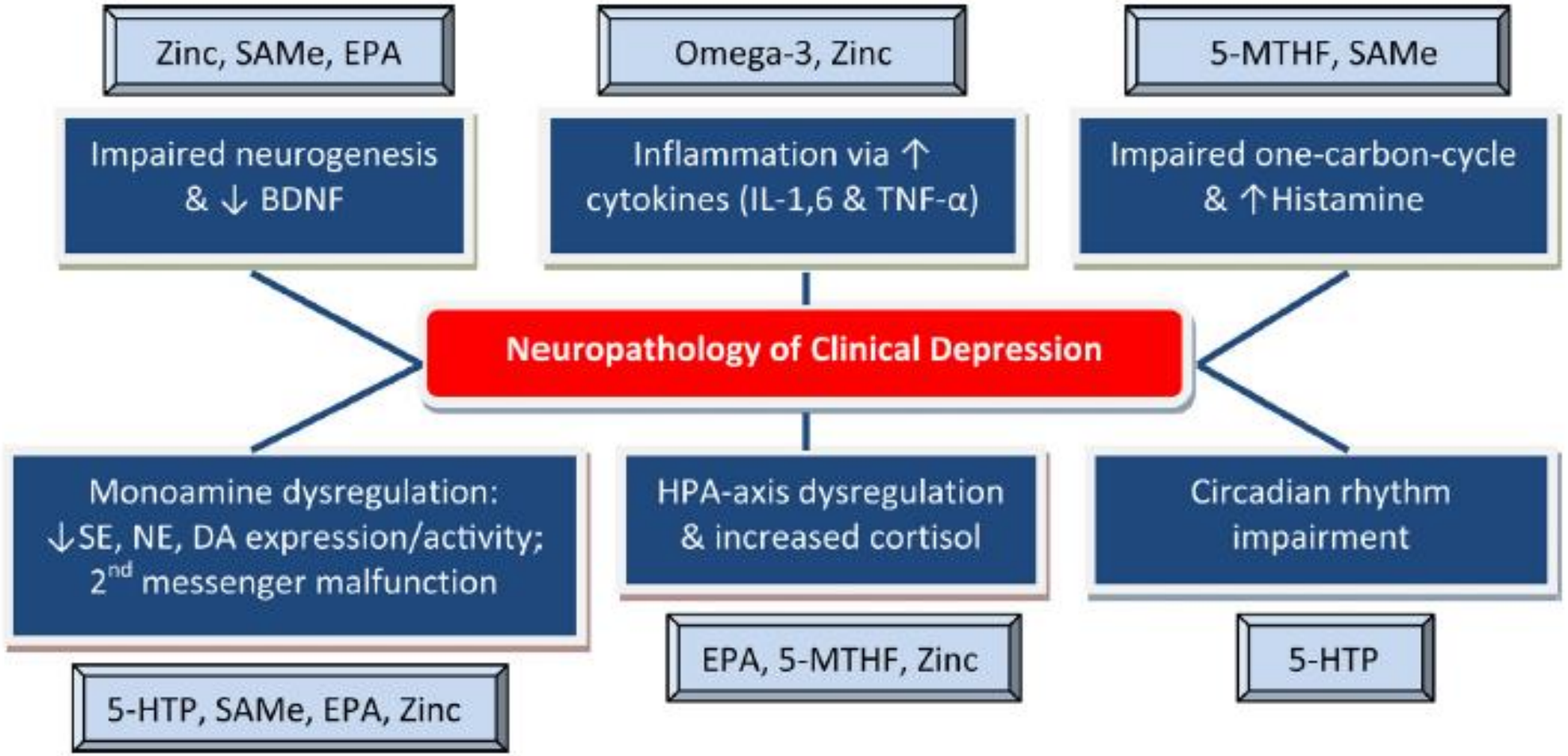


Fig. 1. Pathophysiology of depression and the nutraceuticals modulating these neurochemical pathways.

Sarris et all, An adjunctive antidepressant nutraceutical combination in treating major depression: Study protocol, and clinical considerations - Advances in Integrative Medicine 2 (2015) 49–55

Inflammation: A Contributor to Depressive Comorbidity in Inflammatory Skin Disease

Potential Mechanisms for a Pro-Inflammatory State Contributing to Psychological Effects

There are a number of important mechanisms through which a pro-inflammatory state may contribute to depression, including the psychological effects of circulating mediators and direct effects on the microglia.

There are considerable data showing that elevated levels of circulating cytokines can have a psychological impact. Cytokines such as interleukin (IL)-6 and tumor necrosis factor (TNF)-α can be detected in the serum during major depression, and they exhibit a dose-response relationship with the severity of depression [15, 16].

Furthermore, the activation of the immune system has been shown to induce mood changes which resemble sickness behaviors and overlap with the behavioral symptoms of depression such as anhedonia, anorexia, and social withdrawal [19].

Although inflammation may be local, arising in peripheral organs, pro-inflammatory cytokines such as TNF-α and IL-6, but also dendritic cells, can cross the blood-brain barrier (BBB) and trigger a cascade of events in the central nervous system [21]. The integrity of the BBB can be compromised due to stress, leading to a "leaky BBB" which does not adequately protect the brain from peripheral cytokine infiltration [22]. An overactive stress response [23] and elevated levels of peripheral cytokines can lead to brain cytokine signaling with downstream effects on synaptic function via the actions of the microglia, neurotransmitter metabolism, and neurogenesis [22].

Furthermore, central inflammation has also been associated with oxidative stress and reduced neurogenesis in several brain regions which are implicated in depression including the hippocampus [25–27].

Skin Pharmacol Physiol 2018;31:246–251
DOI: 10.1159/000490002

Psoriasis and Associated Psychiatric Disorders

A Systematic Review on Etiopathogenesis and Clinical Correlation

[a,b]BÁRBARA ISABEL ROQUE CUNHA FERREIRA, MD; [b,c]JOSÉ LUÍS PIO DA COSTA ABREU, MD, PHD;
[a,c]JOSÉ PEDRO GASPAR DOS REIS, MD; [a,c]AMÉRICO MANUEL DA COSTA FIGUEIREDO, MD, PHD

[a]Department of Dermatology, Coimbra Hospital and University Centre, Portugal; [b]Centre for Philosophy of Science, University of Lisbon, Portugal;
[c]Faculty of Medicine of the University of Coimbra

TABLE 3. The etiopathogenesis of depression in psoriasis

DEPRESSION EXACERBATES PSORIASIS	PSORIASIS LEADS TO DEPRESSION	PSORIASIS AND DEPRESSION: SHARED ETIOPATHOGENIC MECHANISMS
• By increasing the levels of pro-inflammatory cytokines, such as IL-6 and TNF-α[36] • By increasing the levels of substance P[30] • Depression modulates itch perception and exacerbates pruritus in psoriasis[23]	• Maladaptive schemas[16,31] • Low sociocultural level; single; female; personal history of depression: higher risk for depression[32,33] • Sleep disorders[9,14] • Sexual disorders[14,26] • Pain and pruritus[3,11,12,14,22,28,29,30] • Disfigurement and stigmatization[20,21] • Lesions on face/genital area[24] • Higher PASI scores[24]	• Abnormal calcium homeostasis[39] • High concentrations of substance P[9,30] • Defect in β-adrenergic function[15] • Low melatonin secretion[40] • High levels of pro-inflammatory cytokines • (IL-1, IL-6, TNF-α)[37]

(*J Clin Aesthet Dermatol.* 2016;9(6):36–43.)

Psoriasis and Associated Psychiatric Disorders

A Systematic Review on Etiopathogenesis and Clinical Correlation

[a,b]BÁRBARA ISABEL ROQUE CUNHA FERREIRA, MD; [b,c]JOSÉ LUÍS PIO DA COSTA ABREU, MD, PHD;
[a,c]JOSÉ PEDRO GASPAR DOS REIS, MD; [a,c]AMÉRICO MANUEL DA COSTA FIGUEIREDO, MD, PHD

[a]Department of Dermatology, Coimbra Hospital and University Centre, Portugal; [b]Centre for Philosophy of Science, University of Lisbon, Portugal;
[c]Faculty of Medicine of the University of Coimbra

TABLE 4. The etiologic factors for sleep and sexual disorders in psoriasis

SLEEP DISORDERS IN PSORIASIS: ETIOLOGY	SEXUAL DISORDERS IN PSORIASIS: ETIOLOGY
Depression[9,37]	Risk factors for cardiovascular disease[3]
Obstructive sleep apnea[9]	Low self-esteem/psychological factors[3,26]
Pain of skin lesions[9,52]	Other psychiatric comorbidities: depression,[11,26] substance dependence, or abuse
Parts of the body affected[8]	Pruritus[11]
Pruritus[9,37]	Psoriatic arthritis[11]
Psoriatic arthritis/joint pain[52]	Side effects of psoriasis treatments[26]

(*J Clin Aesthet Dermatol.* 2016;9(6):36–43.)

Psoriasis: Targets and Therapy

Dovepress
open access to scientific and medical research

Open Access Full Text Article

REVIEW

Psoriasis and sexual dysfunction: links, risks, and management challenges

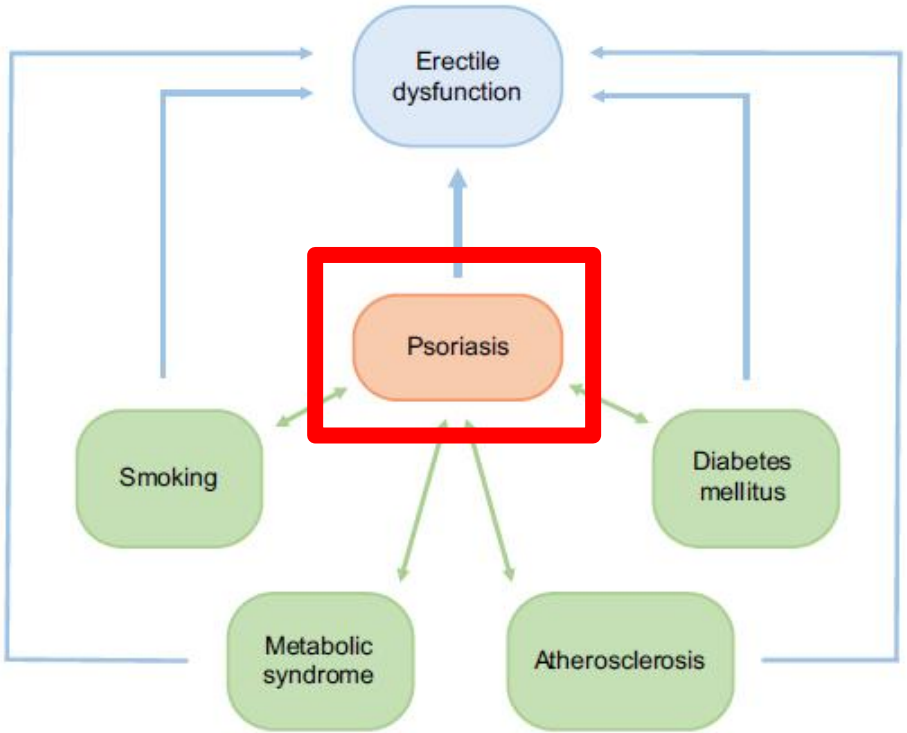


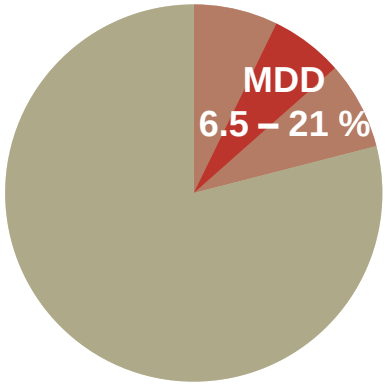
Figure 1 Association between erectile dysfunction, psoriasis, and comorbidities.
Notes: Blue arrows: independent association. Green arrows: comorbidities.

Gleison V Duarte[1]
Humberto Calmon[2]
Gabriela Radel[2]
Maria de Fátima Paim de Oliveira[3]

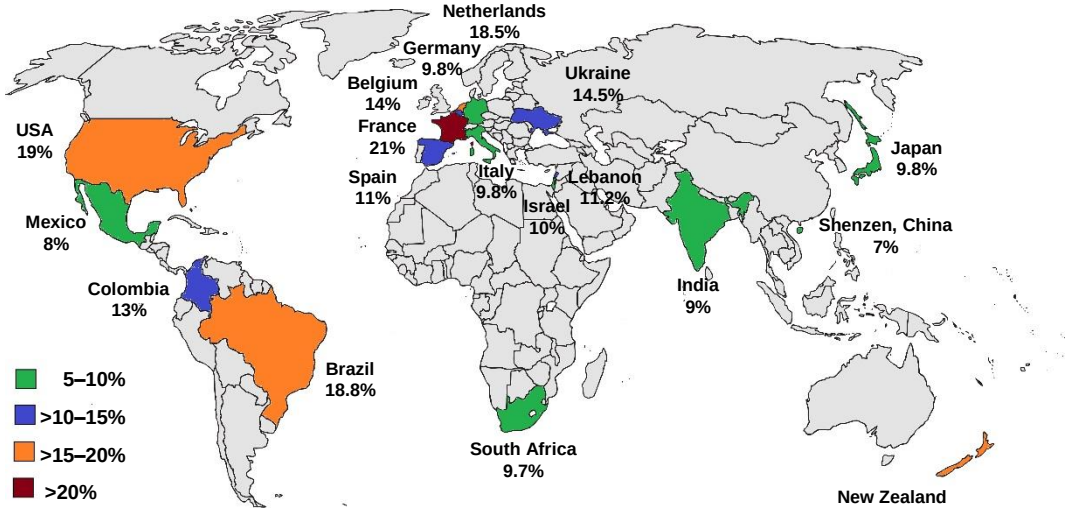
Επιπολασμός της κατάθλιψης…

It is estimated that each year, 6.9% of the EU population suffers from MDD[1]

The lifetime prevalence of MDD is 6.5–21%, depending on the country[2-4]



Mean lifetime prevalence of major depressive episode[4]



*Total high income countries = 14.6%; total low to middle income countries = 11.1%
Only data for countries in the WHO study are presented

(1) Wittchen HU et al. Eur Neuropsychopharmacol 2011;21:655-79; (2) Hasin DS et al. Arch Gen Psychiatry 2005;62:1097-106; (3) Kessler RC et al. Arch Gen Psychiatry 2005;62:593-602; (4) Bromet E et al. BMC Med 2011;9:90

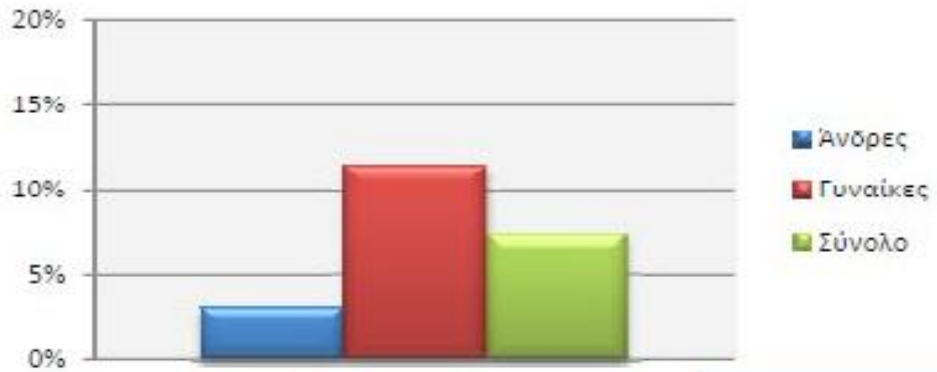
Σχήμα 3: Δείκτες υγείας αντιπροσωπευτικού δείγματος του πληθυσμού στην Ελλάδα, ΥΔΡΙΑ-χρόνια κατάθλιψη

Στο πλαίσιο του προγράμματος ΥΔΡΙΑ οι συμμετέχοντες καλούνταν να συμπληρώσουν ερωτηματολόγιο με κατά πρόσωπο συνέντευξη και απαντούσαν εάν νοσούν ή έχουν νοσήσει από χρόνια κατάθλιψη τους τελευταίους 12 μήνες ή παλαιότερα και αν έχει γίνει διάγνωση από ιατρό.

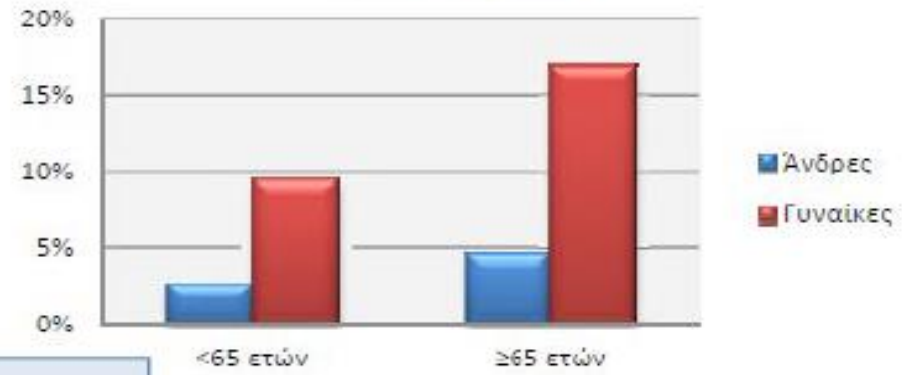
Αποτελέσματα

Αντιπροσωπευτικά του πληθυσμού στην Ελλάδα

Κατά δήλωση επιπολασμός (%) χρόνιας κατάθλιψης ανά φύλο



Κατά δήλωση επιπολασμός (%) χρόνιας κατάθλιψης ανά φύλο και ηλικιακή ομάδα

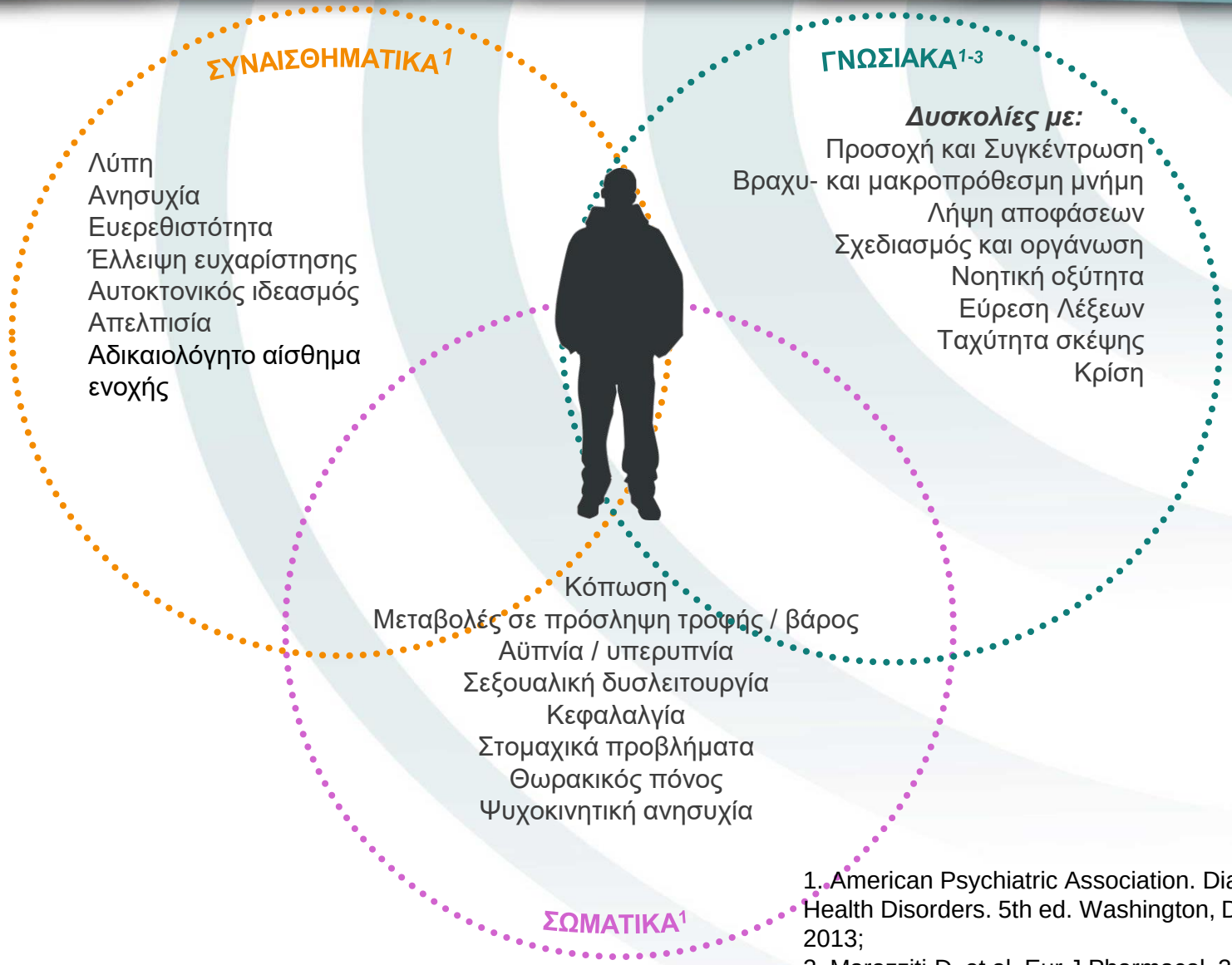


Συμπεράσματα

- ✓ 7% του πληθυσμού στην Ελλάδα έχει ή είχε χρόνια κατάθλιψη, κατά δήλωση
- ✓ Μια στις δέκα γυναίκες ενήλικες μόνιμοι κάτοικοι της Ελλάδας πάσχει ή έπασχε από χρόνια κατάθλιψη, κατά δήλωση
- ✓ Το ποσοστό των γυναικών που δήλωσαν χρόνια κατάθλιψη είναι περίπου 4 φορές μεγαλύτερο από των ανδρών
- ✓ Ο επιπολασμός της χρόνιας κατάθλιψης αυξάνει με την πρόοδο της ηλικίας

Πηγή: Πρόγραμμα ΥΔΡΙΑ, 2014

Η μεγάλη ετερογένεια της κατάθλιψης…



1. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Health Disorders. 5th ed. Washington, DC: American Psychiatric Association; 2013;
2. Marazziti D, et al. Eur J Pharmacol. 2010;626(1):83-86.
3. Hammar A, Ardal G. Front Hum Neurosci. 2009;3:26.

Μείζον Καταθλιπτικό Επεισόδιο: DSM-5

- **Τουλάχιστον 5 από τα ακόλουθα συμπτώματα εμφανίζονται σε διάστημα 2 εβδομάδων και αντιπροσωπεύουν αλλαγή από την προηγούμενη λειτουργία.**

Τουλάχιστον ένα από τα συμπτώματα είναι ένα από τα δύο πρώτα στην παρακάτω λίστα:

- **Καταθλιπτική διάθεση**
- **Μειωμένο ενδιαφέρον / ευχαρίστηση**

- **Αλλαγές του σωματικού βάρους**
- **Διαταραχές ύπνου**
- **Ψυχοκινητική διέγερση/καθυστέρηση**
- **Κόπωση / απώλεια ενέργειας**
- **Αισθήματα απαξίωσης ή υπερβολικές/αδικαιολόγητες ενοχές**
- **Μειωμένη ικανότητα για σκέψη ή συγκέντρωση ή αναποφασιστικότητα**
- **Επανειλημμένες σκέψεις θανάτου/ αυτοκτονικού ιδεασμού**

- **Κλινικά σημαντική θλίψη**

ΕΡΩΤΗΜΑΤΟΛΟΓΙΟ ΥΓΕΙΑΣ ΑΣΘΕΝΟΥΣ (PHQ-9)

Τις τελευταίες 2 εβδομάδες πόσο συχνά ενοχληθήκατε απ' οποιοδήποτε από τα παρακάτω προβλήματα; *(Υποδείξτε την απάντησή σας με ένα "✔")*	Καθόλου	Αρκετές μέρες	Περισσότερες από τις μισές μέρες	Σχεδόν κάθε μέρα
1. Μικρό ενδιαφέρον ή λίγη απόλαυση στις δραστηριότητές μου	0	1	2	3
2. Νιώθετε καταβεβλημένος(η), κατατεθλιμμένος(η) ή απελπισμένος(η)	0	1	2	3
3. Έχετε πρόβλημα να αποκοιμηθείτε ή να συνεχίσετε τον ύπνο σας ή κοιμάστε υπερβολικά	0	1	2	3
4. Νιώθετε κουρασμένος(η) ή έχετε λίγη ενέργεια	0	1	2	3
5. Έχετε λίγη όρεξη ή τρώτε υπερβολικά	0	1	2	3
6. Νιώθετε άσχημα για τον εαυτό σας ή ότι έχετε αποτύχει ή ότι έχετε απογοητεύσει τον εαυτό σας ή την οικογένειά σας	0	1	2	3
7. Έχετε πρόβλημα συγκέντρωσης σε κάποιες ενέργειες, όπως όταν διαβάζετε την εφημερίδα ή όταν παρακολουθείτε τηλεόραση	0	1	2	3
8. Κινείστε ή μιλάτε τόσο αργά που άλλοι άνθρωποι θα το παρατηρούσαν Ή το αντίθετο – είστε τόσο ανήσυχος(η) ή νευρικός(ή), που κινείστε πολύ περισσότερο από το συνηθισμένο	0	1	2	3
9. Σκεπτόσαστε ότι θα ήταν καλύτερα αν είχατε πεθάνει ή σκεπτόσαστε να προκαλέσετε κακό στον εαυτό σας με κάποιο τρόπο	0	1	2	3

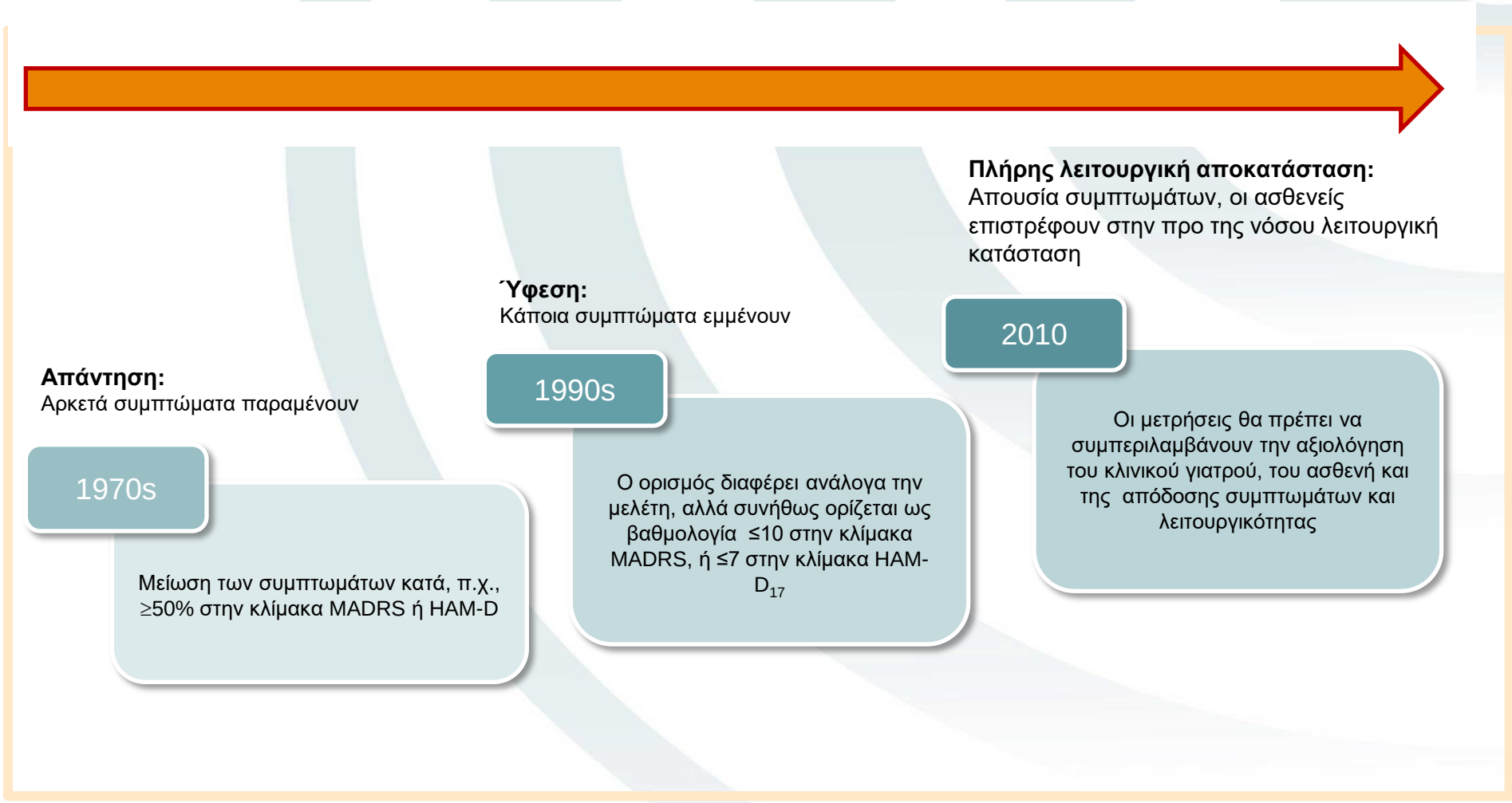
FOR OFFICE CODING *0* + _____ + _____ + _____

=Total Score: _____

Εάν επιλέξατε **κάποια** προβλήματα, πόση **δυσκολία** προκάλεσαν τα προβλήματα αυτά στη δουλειά σας, στις οικιακές εργασίες σας ή στην επικοινωνία σας με άλλα άτομα;

Καμία δυσκολία	Μερική δυσκολία	Μεγάλη δυσκολία	Υπερβολική δυσκολία
☐	☐	☐	☐

Θεραπευτικός στόχος στην κατάθλιψη…

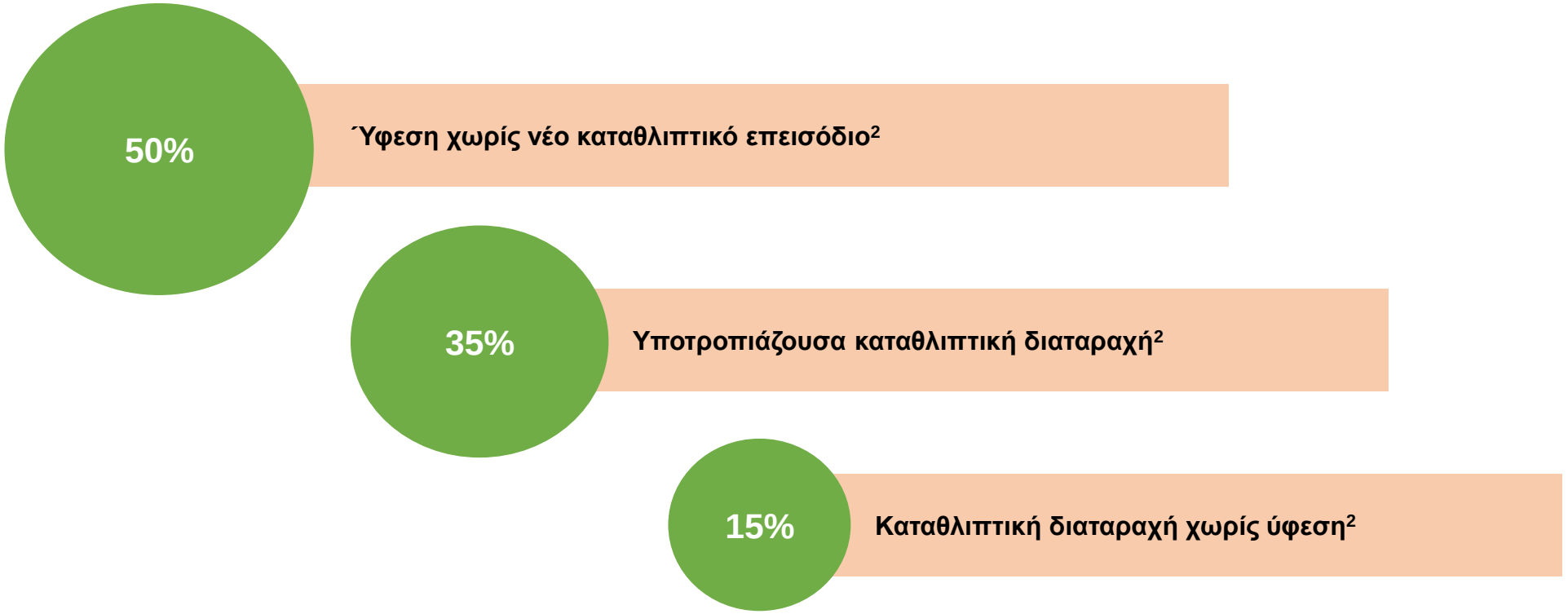


McIntyre & O'Donovan. Can J Psychiatry 2004;49(3 Suppl 1):10S–16S;

MADRS=Montgomery–Åsberg Depression Rating Scale; HAM-D=Hamilton Rating Scale for Depression;
HAM-D_{17}=17-item Hamilton Rating Scale for Depression

Η κατάθλιψη είναι μια σύνθετη και συχνά υποτροπιάζουσα διαταραχή

Πορεία της κατάθλιψης μετά το πρώτο επεισόδιο[1]:



1. Kupfer DJ. J Clin Psychiatry 1991;52(suppl):28–34. 2. Eaton WW et al. Arch Gen Psychiatry 2008;65:513–520

From: **Association of Mental Disorders With Subsequent Chronic Physical Conditions: World Mental Health Surveys From 17 Countries**

JAMA Psychiatry. Published online December 23, 2015.1-9 doi:10.1001/jamapsychiatry.2015.2688

Table 2. Bivariate Associations Between *DSM-IV* Mental Disorders and the Subsequent Onset or Diagnosis of Chronic Physical Conditions

Mental Disorder[a]	Chronic Physical Condition, OR (95% CI)									
	Arthritis	Any Chronic Pain[b]	Heart Disease	Stroke	Hypertension	Diabetes Mellitus	Asthma	Chronic Lung Disease	Peptic Ulcer	Cancer
Mood disorder										
Major depressive episode/dysthymia	1.6 (1.5-1.8)[c]	1.7 (1.6-1.8)[c]	1.5 (1.3-1.8)[c]	1.6 (1.3-2.1)[c]	1.4 (1.2-1.5)[c]	1.4 (1.2-1.6)[c]	1.5 (1.3-1.8)[c]	2.1 (1.6-2.8)[c]	1.7 (1.5-1.9)[c]	1.2 (1.0-1.5)[c]
Bipolar disorder (broad)	1.7 (1.4-2.0)[c]	1.8 (1.6-2.1)[c]	1.6 (1.1-2.4)[c]	1.9 (1.1-3.1)[c]	1.4 (1.1-1.8)[c]	1.7 (1.2-2.3)[c]	2.4 (1.7-3.3)[c]	2.3 (1.5-3.7)[c]	1.8 (1.4-2.3)[c]	1.5 (1.0-2.2)
Anxiety disorder										
Panic disorder	1.5 (1.3-1.8)[c]	1.9 (1.6-2.1)[c]	2.1 (1.6-2.7)[c]	1.9 (1.1-3.1)[c]	1.7 (1.4-2.0)[c]	1.8 (1.3-2.4)[c]	1.9 (1.3-2.7)[c]	2.2 (1.4-3.3)[c]	1.9 (1.4-2.4)[c]	1.6 (1.2-2.1)[c]
Generalized anxiety disorder	1.8 (1.6-2.0)[c]	1.9 (1.8-2.2)[c]	1.4 (1.1-1.7)[c]	1.5 (1.0-2.3)[c]	1.4 (1.2-1.5)[c]	1.3 (1.0-1.6)[c]	1.7 (1.4-2.2)[c]	2.5 (1.8-3.5)[c]	1.5 (1.3-1.8)[c]	1.0 (0.8-1.3)
Social phobia	1.5 (1.4-1.7)[c]	1.8 (1.7-2.0)[c]	1.5 (1.2-1.9)[c]	1.8 (1.3-2.5)[c]	1.5 (1.3-1.6)[c]	1.3 (1.1-1.6)[c]	1.4 (1.1-1.7)[c]	1.9 (1.4-2.6)[c]	1.8 (1.6-2.2)[c]	1.1 (0.9-1.3)[c]
Specific phobia	1.5 (1.4-1.7)[c]	1.8 (1.7-1.9)[c]	1.8 (1.5-2.1)[c]	1.6 (1.3-2.1)[c]	1.5 (1.3-1.6)[c]	1.4 (1.1-1.6)[c]	1.5 (1.3-1.8)[c]	1.6 (1.2-2.1)[c]	1.8 (1.6-2.1)[c]	1.4 (1.2-1.6)[c]
Agoraphobia without panic	1.4 (1.1-1.8)	1.8 (1.4-2.2)	1.3 (0.8-2.0)	2.2 (1.0-4.5)	1.6 (1.2-2.0)	1.6 (1.2-2.4)	1.3 (0.9-2.1)	2.0 (1.1-3.6)	1.6 (1.1-2.4)	1.3 (0.8-2.1)
Posttraumatic stress disorder	1.8 (1.6-2.1)[c]	1.9 (1.7-2.2)[c]	2.1 (1.6-2.7)[c]	1.7 (1.1-2.6)[c]	1.3 (1.1-1.6)[c]	1.4 (1.0-1.9)[c]	1.9 (1.4-2.5)[c]	1.6 (1.1-2.3)[c]	2.3 (1.9-2.9)[c]	1.3 (1.0-1.8)[c]
Obsessive-compulsive disorder	1.4 (1.0-1.9)[c]	2.1 (1.7-2.6)[c]	1.6 (1.1-2.5)[c]	1.5 (0.6-3.8)	1.3 (0.9-1.8)	1.2 (0.6-2.3)	0.7 (0.4-1.5)	1.9 (0.8-4.5)	2.0 (1.2-3.6)[c]	1.8 (1.0-3.2)
Impulse control disorder										
Intermittent explosive disorder	1.6 (1.4-2.0)[c]	2.3 (2.0-2.6)[c]	1.6 (1.1-2.4)[c]	1.9 (1.1-3.3)[c]	1.5 (1.2-1.8)[c]	1.8 (1.3-2.5)[c]	1.3 (0.9-2.0)	3.0 (2.0-4.7)[c]	2.0 (1.5-2.5)[c]	1.5 (1.0-2.2)[c]
Bulimia nervosa	1.5 (1.0-2.2)[c]	2.1 (1.6-2.7)[c]	1.9 (0.9-3.9)	3.3 (1.4-8.0)[c]	2.3 (1.7-3.2)[c]	3.6 (2.0-6.6)[c]	1.3 (0.8-2.4)	0.7 (0.2-2.3)	1.6 (0.9-2.9)	1.6 (0.8-3.0)
Binge-eating disorder	1.7 (1.3-2.3)[c]	2.0 (1.5-2.6)[c]	1.4 (0.8-2.6)	1.5 (0.7-3.4)	2.0 (1.4-2.7)[c]	3.4 (2.0-5.9)[c]	2.1 (1.4-3.2)[c]	1.4 (0.7-2.5)	1.6 (1.0-2.5)[c]	1.6 (0.9-3.0)
Substance use disorder										
Alcohol abuse	1.6 (1.4-1.8)[c]	1.4 (1.3-1.6)[c]	1.7 (1.4-2.1)[c]	2.1 (1.5-3.0)[c]	1.6 (1.4-1.8)[c]	1.3 (1.1-1.6)[c]	1.6 (1.3-2.0)[c]	2.4 (1.8-3.2)[c]	1.6 (1.4-1.9)[c]	1.4 (1.1-1.8)[c]
Alcohol dependence	1.7 (1.4-2.0)[c]	1.6 (1.4-1.9)[c]	2.3 (1.8-3.0)[c]	2.8 (1.5-5.0)[c]	1.8 (1.5-2.1)[c]	1.5 (1.1-2.1)[c]	2.1 (1.5-2.8)[c]	2.0 (1.3-3.2)[c]	1.9 (1.5-2.4)[c]	1.4 (1.0-2.0)
Drug abuse	1.9 (1.6-2.2)[c]	1.6 (1.4-1.9)[c]	2.2 (1.6-3.0)[c]	1.9 (1.1-3.3)[c]	1.9 (1.6-2.2)[c]	1.8 (1.2-2.5)[c]	1.4 (1.0-2.0)	1.9 (1.3-2.8)[c]	2.0 (1.6-2.5)[c]	1.3 (0.9-2.1)
Drug dependence	2.1 (1.7-2.7)[c]	1.8 (1.4-2.3)[c]	1.7 (1.1-2.6)[c]	1.9 (0.9-3.9)	2.1 (1.6-2.8)[c]	2.5 (1.5-4.1)[c]	1.2 (0.7-2.0)	1.7 (0.9-3.3)	2.3 (1.8-3.1)[c]	1.4 (0.8-2.7)

Abbreviation: OR, odds ratio.

[a] Each mental disorder was estimated as a predictor of the physical condition onset in a separate discrete time survival model controlling for age cohorts, sex, person-years, country, smoking (current, ever, or never), and respondent's educational level.

[b] Respondent reported any of the following: chronic back or neck pain, frequent or severe headaches, and other chronic pain condition.

[c] Significant at $P < .05$, 2-sided test.

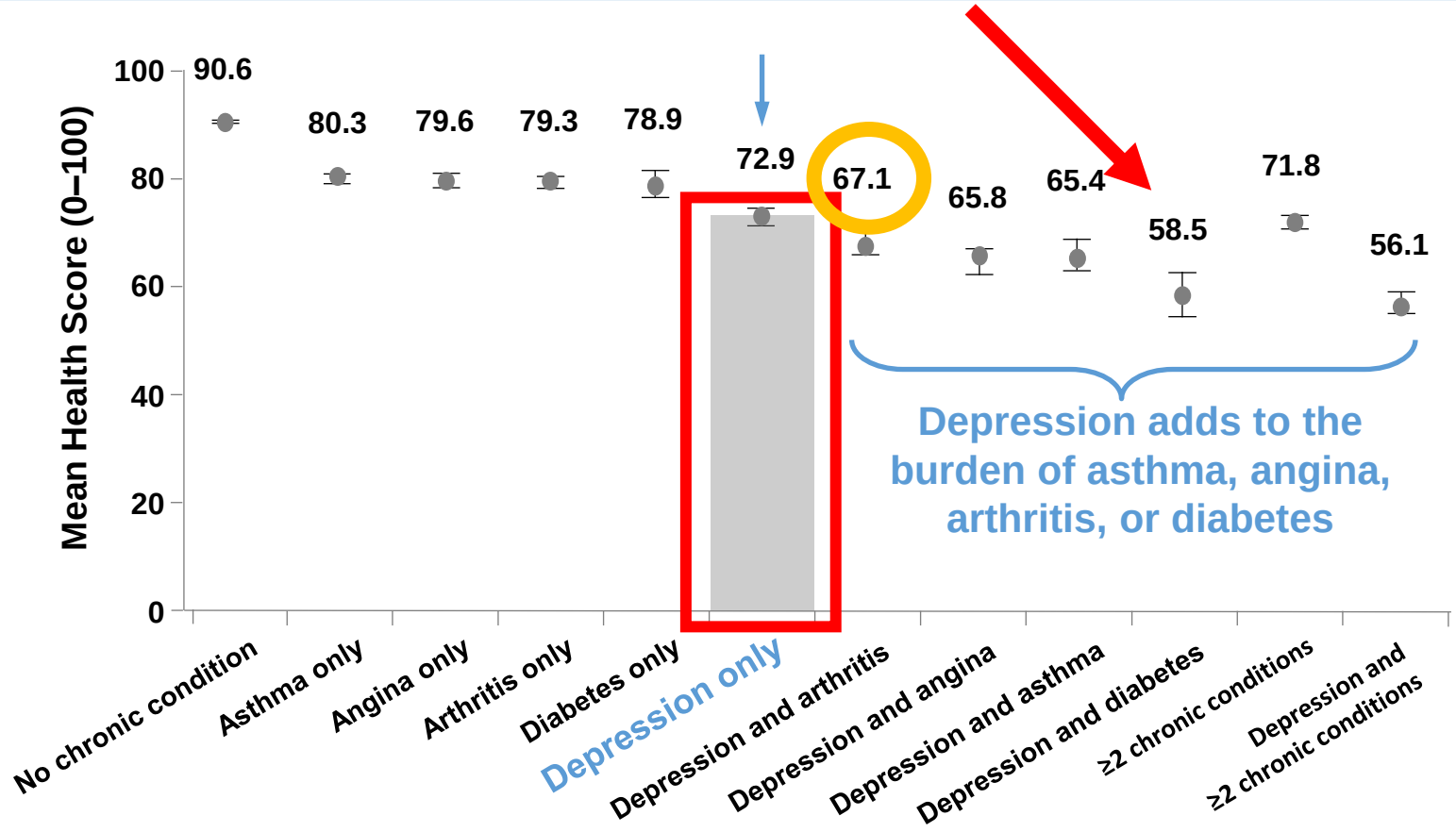
From: **Association of Mental Disorders With Subsequent Chronic Physical Conditions: World Mental Health Surveys From 17 Countries**

JAMA Psychiatry. Published online December 23, 2015.1-9 doi:10.1001/jamapsychiatry.2015.2688

Table 2. Bivariate Associations Between *DSM-IV* Mental Disorders and the Subsequent Onset or Diagnosis of Chronic Physical Conditions

	Chronic Physical Condition, OR (95% CI)									
Mental Disorder[a]	Arthritis	Any Chronic Pain[b]	Heart Disease	Stroke	Hypertension	Diabetes Mellitus	Asthma	Chronic Lung Disease	Peptic Ulcer	Cancer
Mood disorder										
Major depressive episode/dysthymia	1.6 (1.5-1.8)[c]	1.7 (1.6-1.8)[c]	1.5 (1.3-1.8)[c]	1.6 (1.3-2.1)[c]	1.4 (1.2-1.5)[c]	1.4 (1.2-1.6)[c]	1.5 (1.3-1.8)[c]	2.1 (1.6-2.8)[c]	1.7 (1.5-1.9)[c]	1.2 (1.0-1.5)[c]

Η κατάθλιψη επηρεάζει συνολικά την υγεία των ασθενών



Depression is associated with poorer overall health scores than arthritis or diabetes and significantly adds to the burden of other chronic conditions

- Adapted from Moussavi S, et al. Lancet. 2007;370:851-8.

Η πορεία της κατάθλιψης στο χρόνο…

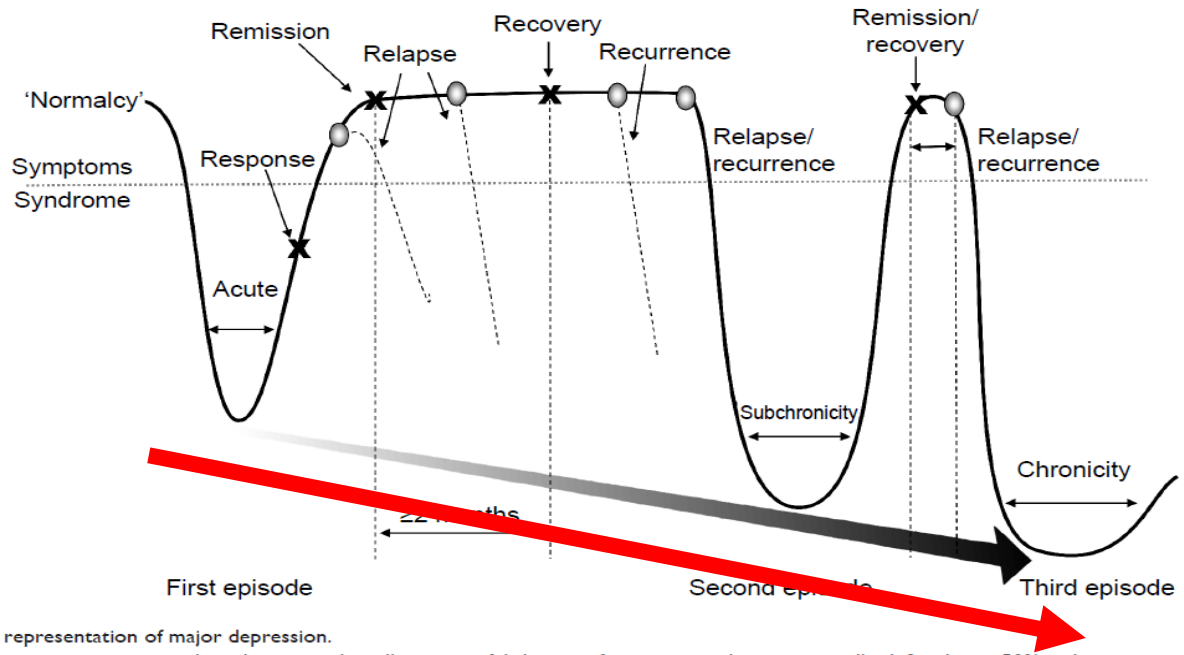


Figure 1 Schematic representation of major depression.
Notes: Response to treatment occurs when there is a clinically meaningful degree of symptom reduction, typically defined as ≥50% reduction in pretreatment symptom severity. Remission occurs when the symptoms of the MDE are absent or close to it. Without validated biomarkers, recovery may not be clinically distinguishable from remission, but is implied after an extended asymptomatic period (≥2 months), following which the likelihood of an MDE is reduced. A relapse is defined as the return of the initial MDE following remission, while recurrence is defined as the development of a new MDE following the onset of recovery. Relapses or recurring MDEs of increasing severity and longer duration, shorter remission periods, and reduced therapeutic response over time contribute to the progression and chronicity of major depression. Adapted from Journal of Clinical Psychiatry. 1991, 52, Long-term treatment of depression. *Kupfer DJ*. 28–34.[21] Adapted © from Sibille E, French B. Biological substrates underpinning diagnosis of major depression. *International Journal of Neuropsychopharmacolgy*. 2013;16(8):1893–1909 by permission of Oxford University Press.[22]
Abbreviation: MDE, major depressive episode.

Αποτελεσματικότητα και αποδοχή θεραπείας από ασθενείς

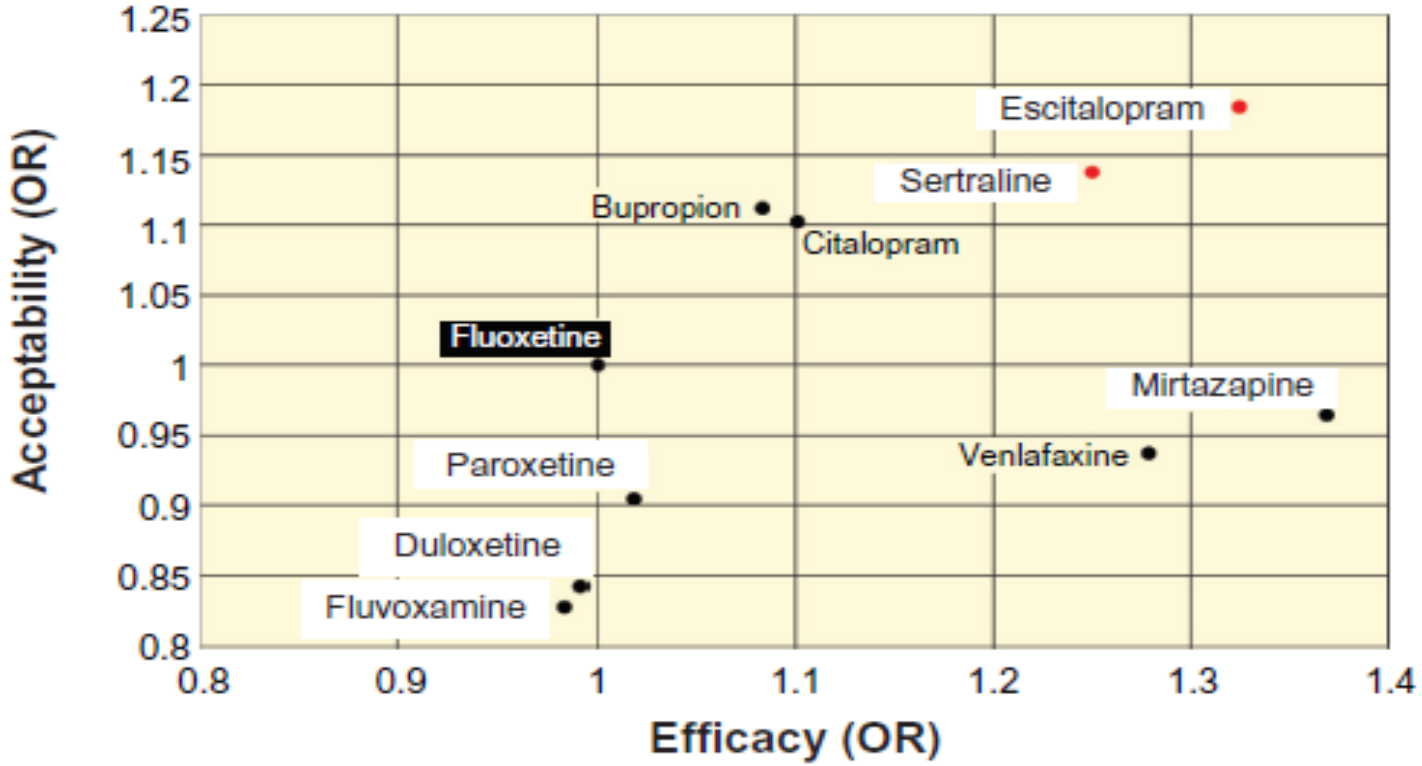
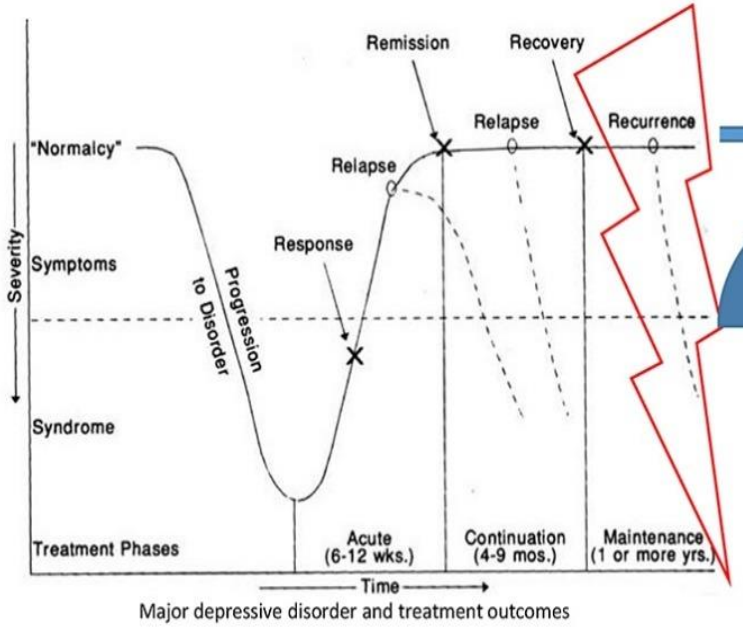


Figure 5 Efficacy and patient acceptability of new antidepressant drugs.
Notes: The odds ratios (OR) of acceptability and efficacy were based on a value of 1 for fluoxetine. Acceptability of escitalopram was highest among the new antidepressant drugs examined. Copyright © 2009, The Family Physician's Inquiries Network (FPIN). Adapted with permission from Patrick G, Combs G, Gavagan T. Initiating antidepressant therapy? Try these 2 drugs first. *J Fam Pract.* 2009;58(7):365–369.[52]
Abbreviation: OR, odds ratio.

Απώλεια αποτελεσματικότητας αντικαταθλιπτικών



Major depressive disorder and treatment outcomes

Pharmacological Research 139 (2019) 494–502

Enduring maintenance

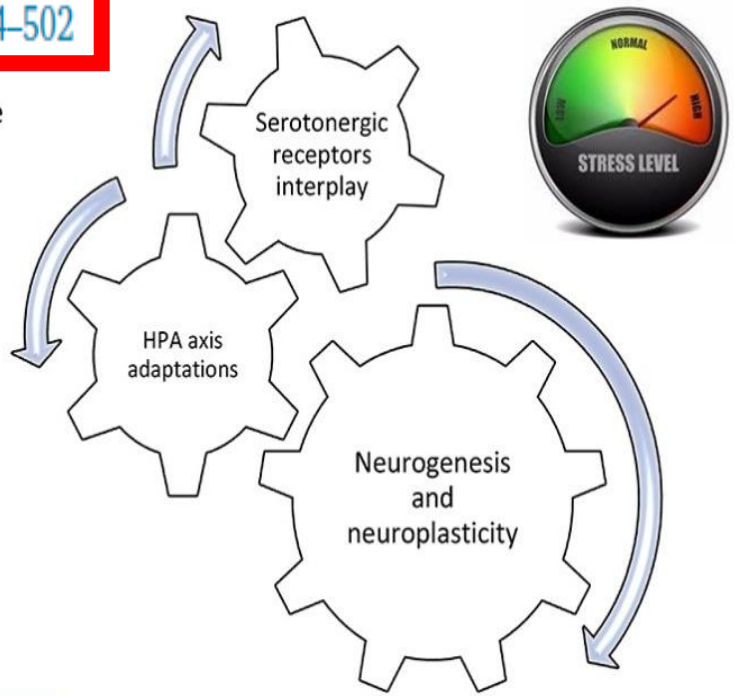
Loss of efficacy during **antidepressant** drug treatment

Events potentially associated with loss of efficacy of the antidepressant drugs

- Rapid cycling
- Polypharmacy
- Manic switch
- Sub-optimal treatment adherence
- Suicide

- Tolerance
- Tachyphylaxis
- Poop-out/up/wear-off response

Inconsistency of the operational definitions appraised in the literature



Unmet needs and proposals for future research: consensus about reliable operational definitions towards the identification of reliable biomarkers.

Potential clinical management: avoid overexposure to unnecessary/protracted medications and consider sub-threshold bipolarity; promote psychoeducation and manage medical and psychiatric comorbidities. Consider augmentation with lithium and/or atypical antipsychotics.

RHEUMATOLOGY

Rheumatology 2018;57:835–843
doi:10.1093/rheumatology/kex528
Advance Access publication 13 February 2018

Original article

The relationship between depression and biologic treatment response in rheumatoid arthritis: An analysis of the British Society for Rheumatology Biologics Register

Faith Matcham[1], Rebecca Davies[2,3], Matthew Hotopf[1,4], Kimme L. Hyrich[2,3], Sam Norton[5,6], Sophia Steer[6] and James Galloway[6]

Results. Depression symptoms at biologic treatment initiation were associated with 20–40% reduced odds of achieving a good treatment response at 1 year. Depressive symptoms at baseline also associated with reduced improvement in disease activity over the course of follow-up. Patients with a history of depression or reporting symptoms of depression according to the EuroQol five-dimension scale showed reduced improvement in tender and swollen joints, patient global assessment and ESR over 1-year follow-up. Patients with depression symptoms according to the 36-item Short Form showed reduced improvement in tender and swollen joints, but not ESR or patient global assessment.

Conclusion. Experiencing symptoms of depression at the start of biologics treatment may reduce the odds of achieving a good treatment response, and reduce improvement in disease activity over time. Depression should be managed as part of routine clinical care to optimize treatment outcomes.

Anti-cytokine agents for anhedonia: targeting inflammation and the immune system to treat dimensional disturbances in depression

Ther Adv Psychopharmacol
2018, Vol. 8(12) 337–348
DOI: 10.1177/2045125318791944

Yena Lee, Mehala Subramaniapillai, Elisa Brietzke, Rodrigo B. Mansur, Roger C. Ho, Samantha J. Yim and Roger S. McIntyre

Correspondence to:
Roger S. McIntyre

Approximately 15–22% of individuals with chronic inflammatory conditions (e.g. rheumatoid arthritis, systemic lupus erythematosus) present with clinically significant depressive symptoms.[19,20]

engagement.[97–100] In contrast, preliminary evidence suggests that biologics (e.g. monoclonal antibodies) that specifically target individual cytokines (e.g. TNF-alpha) are effective in reducing depressive symptoms without off-target effects. For example, a recent meta-analysis (n = 2370) of seven randomized, controlled trials of anticytokine agents (e.g. adalimumab, etanercept, tocilizumab, infliximab) in chronic inflammatory conditions (e.g. rheumatoid arthritis) reported significant antidepressant efficacy of moderate effect size [standardized mean difference (SMD) = 0.40, 95% confidence interval (CI) = 0.22, 0.59].[100]

Anti-cytokine agents for anhedonia: targeting inflammation and the immune system to treat dimensional disturbances in depression

Ther Adv Psychopharmacol
2018, Vol. 8(12) 337–348
DOI: 10.1177/2045125318791944

Yena Lee, Mehala Subramaniapillai, Elisa Brietzke, Rodrigo B. Mansur, Roger C. Ho, Samantha J. Yim and Roger S. McIntyre

Correspondence to:
Roger S. McIntyre

Similarly, individuals with mood disorders are more likely to have or develop metabolic and inflammatory comorbidities (e.g. diabetes mellitus, metabolic syndrome, central obesity, hypertension, cardiovascular disease, autoimmune disorders) when compared with the general population.[21–25] Diabetes mellitus and mood disorders are bidirectionally associated with a synergy index of 2.2.[26] Populations with an immune-mediated disease (e.g. inflammatory bowel disease, multiple sclerosis, rheumatoid arthritis) also have a higher incidence of major depressive, anxiety, and bipolar disorders.[25] Chronic, aberrant activation of the

clinical trial.[107,108] Infliximab is a chimeric monoclonal antibody that targets TNF-alpha, is administered intravenously, and is approved by the FDA and Health Canada for the treatment of several rheumatic disorders (e.g. rheumatoid arthritis, Crohn's disease, ankylosing spondylitis, psoriatic arthritis, and ulcerative colitis).[109] In a randomized, double-blinded, placebo-controlled trial of infliximab in depressed subjects meeting diagnostic criteria for a current MDE as part of treatment-resistant MDD ($n = 51$) or bipolar disorder ($n = 9$), Raison and colleagues reported that infliximab significantly improved depressive symptoms in subjects with baseline inflammatory activation (i.e. hs-CRP levels of >5 mg/l), but not in subjects without baseline inflammatory activation (i.e. hs-CRP $\leqslant$ 5 mg/l); in fact, subjects without baseline inflammatory activation were more likely to benefit from placebo than active treatment.[107] A case report of antidepressant efficacy

ORIGINAL ARTICLE

Depression Is Associated with an Increased Risk of Psoriatic Arthritis among Patients with Psoriasis: A Population-Based Study

Ryan T. Lewinson[1,2], Isabelle A. Vallerand[1,3], Mark W. Lowerison[3], Laurie M. Parsons[4], Alexandra D. Frolkis[1,3], Gilaad G. Kaplan[3,5], Andrew G.M. Bulloch[3,6,7], Mark G. Swain[5], Scott B. Patten[3,6] and Cheryl Barnabe[3,8]

The factors that contribute to the development of psoriatic arthritis (PsA) among patients with psoriasis are not well known; however, systemic inflammation is believed to be important. On the basis of recent laboratory work demonstrating that major depressive disorder (MDD) is associated with increased systemic inflammation, we hypothesized that patients with psoriasis who develop MDD are at increased risk of subsequently developing PsA. We utilized The Health Improvement Network, a primary care medical records database, to identify 73,447 individuals with psoriasis. Patients were followed up to 25 years until the development of the primary outcome of PsA or the censor date. The exposure of interest was the development of MDD. Cox proportional-hazards models showed that patients with psoriasis who developed MDD were at significantly increased risk of subsequently developing PsA compared with patients who did not develop MDD, even after accounting for numerous covariates (hazard ratio 1.37, 95% confidence interval 1.05–1.80, $P = 0.021$). This result was maintained through numerous sensitivity analyses. These data support the hypothesis that MDD increases the risk of developing PsA among patients with psoriasis, suggesting a need for heightened prevention and management of MDD in patients with psoriasis.

Journal of Investigative Dermatology (2017) **137**, 828–835; doi:10.1016/j.jid.2016.11.032

Seminars in Arthritis and Rheumatism 47 (2017) 351–360

Contents lists available at ScienceDirect

Seminars in Arthritis and Rheumatism

journal homepage: www.elsevier.com/locate/semarthrit

The psychosocial burden of psoriatic arthritis

M. Elaine Husni, MD, MPH[a,*], Joseph F. Merola, MD, MMSc[b], Sara Davin, PsyD, MPH[a]

[a] Cleveland Clinic, Main Campus, 9500 Euclid Ave, Cleveland, OH 44195
[b] Brigham and Women's Hospital and Harvard Medical School, Boston, MA

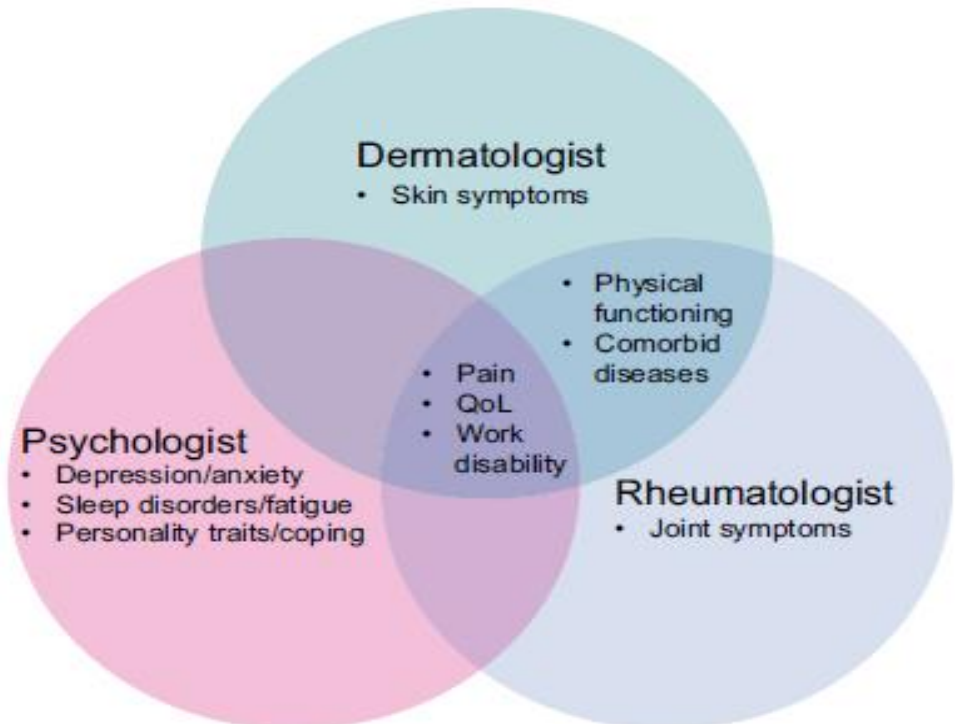
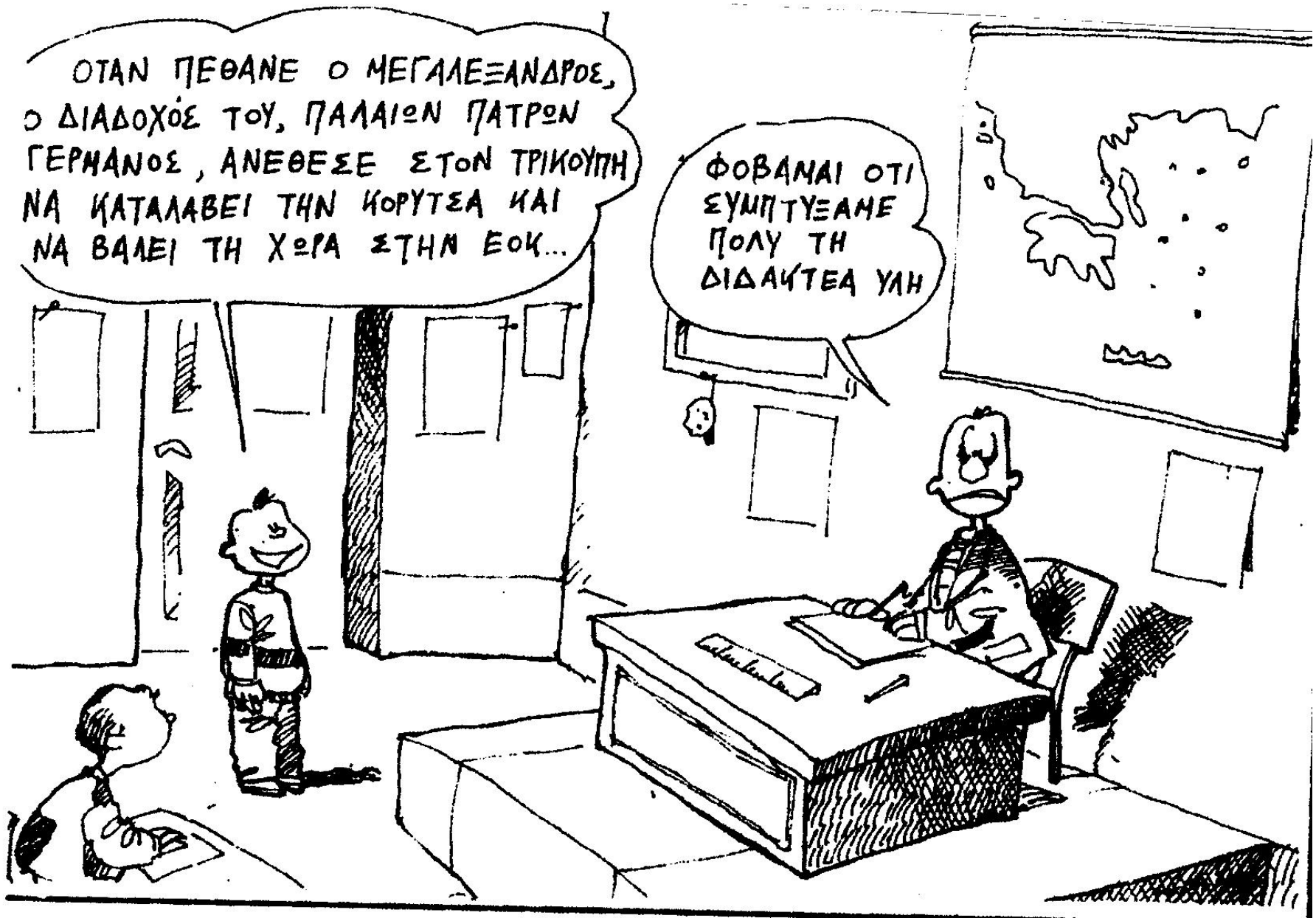


Fig. Integrated approach to treatment of patients with psoriatic arthritis (PsA) and its psychosocial burden.


ΟΤΑΝ ΠΕΘΑΝΕ Ο ΜΕΓΑΛΕΞΑΝΔΡΟΣ, Ο ΔΙΑΔΟΧΟΣ ΤΟΥ, ΠΑΛΑΙΩΝ ΠΑΤΡΩΝ ΓΕΡΜΑΝΟΣ, ΑΝΕΘΕΣΕ ΣΤΟΝ ΤΡΙΚΟΥΠΗ ΝΑ ΚΑΤΑΛΑΒΕΙ ΤΗΝ ΚΟΡΥΤΣΑ ΚΑΙ ΝΑ ΒΑΛΕΙ ΤΗ ΧΩΡΑ ΣΤΗΝ ΕΟΚ...
ΦΟΒΑΜΑΙ ΟΤΙ ΣΥΜΠΤΥΞΑΜΕ ΠΟΛΥ ΤΗ ΔΙΔΑΚΤΕΑ ΥΛΗ

Ευχαριστώ για το χρόνο
και την προσοχή σας!

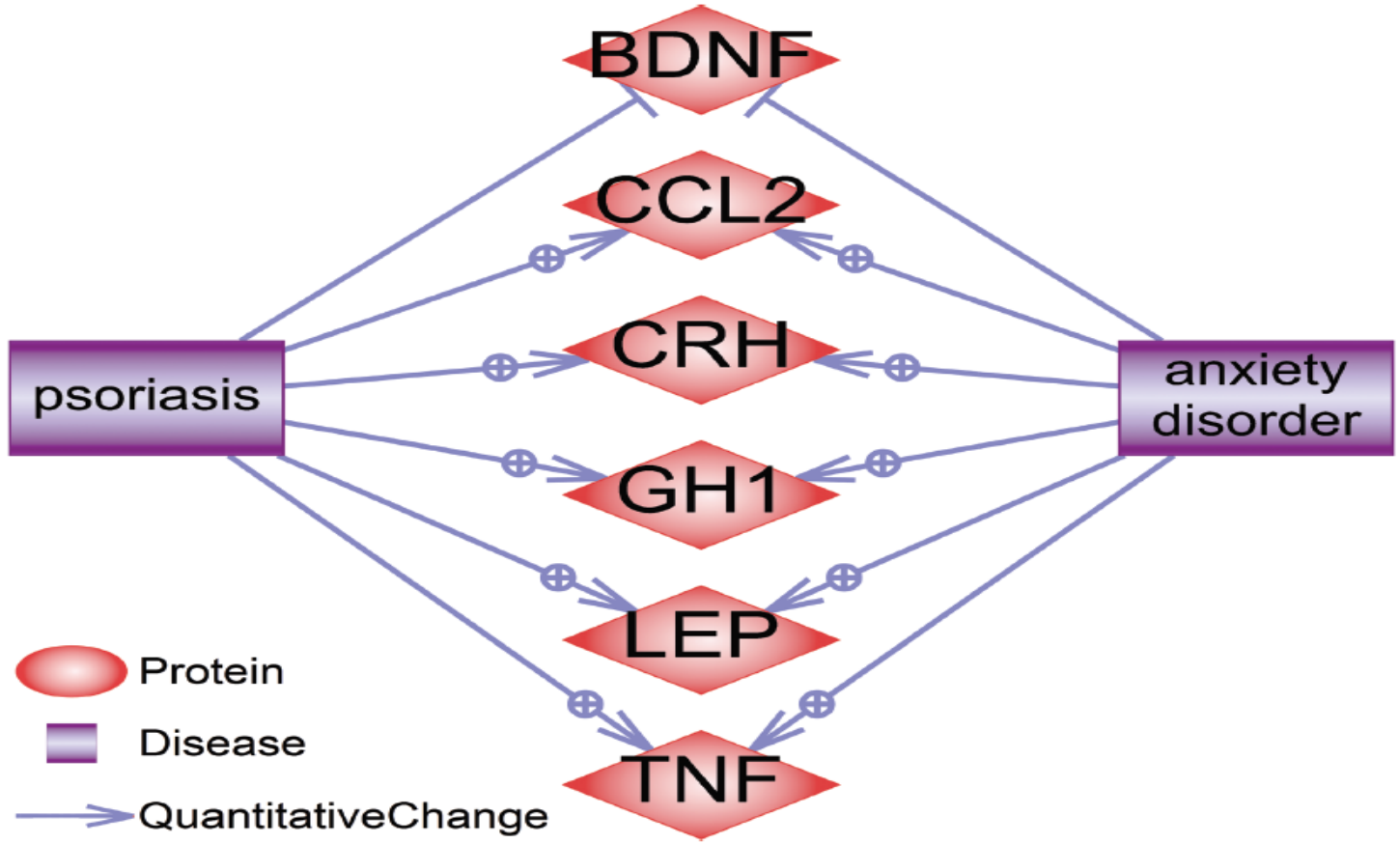


Figure 1 | Proteins with altered expression linked with both psoriasis and anxiety disorders.

Table 1 | Proteins and their links to psoriasis and anxiety disorder in alphabetical order. Functions are listed according to NCBI (https://www.ncbi.nlm.nih.gov/gene).

Gene, description	Link to psoriasis	Link to anxiety disorder
BDNF (brain-derived neurotrophic factor) responsible for growth and homeostasis of brain neurons	Lowered in patients with psoriasis, depression (21), chronic stress (22)	Lowered in patients with anxiety disorders (23–26)
CCL2 (chemokine (C-C motif) ligand 2) activates chemotaxis in monocytes and basophils	Significant increase in serum of patients with psoriasis (27, 28)	Increased in patients with anxiety disorder (29)
GH1 (growth hormone) required for control of body height	Increased in patients with skin diseases, including psoriasis (30)	Increased in patients with stress and anxiety disorder (31)
CRH (corticotropin-releasing hormone) is synthesized in response to stress and stimulates release of adrenocorticotropin	Significant increase in serum of patients with psoriasis (32)	Increased in patients with anxiety disorder (31, 33, 34)
LEP (leptin) is secreted by adipocytes, regulates fat and energy metabolism, as well as some	Increased in patients with psoriasis (35–42)	Increased in patients with anxiety disorder (43)

Acta Dermatovenerol APA

Acta Dermatovenerologica
Alpina, Pannonica et Adriatica

2018;27:179-183
doi: 10.15570/actaapa.2018.38

Psychodermatology: a molecular link between psoriasis and anxiety disorder

Eugene Klimov[1,2,3]✉, Artemii Tretiakov[1], Olga Rudko[1], Anna Soboleva[4], Ivan Danilin[5], Irina Korsunskaya[4], Vladimir Sobolev[2,4,6]

Abstract

This article describes premises for the development of psychodermatology. An analysis of research literature and data is presented based on the example of psoriasis and anxiety disorder. Protein molecules with altered concentrations in patients with psoriasis and anxiety disorder compared to controls are identified (chemokine [C-C motif] ligand 2, corticotropin-release hormone, growth hormone 1, leptin, and tumor necrosis factor with increased concentration and brain-derived neurotrophic factor with decreased concentration). All molecules are secretory peptides. In the future, the information obtained may make it possible to pursue an in-depth study of the molecular mechanisms underlying psychodermatology.

Keywords: psychodermatology, psoriasis, anxiety disorder, signaling pathways, peptides

Received: 30 March 2018 | Returned for modification: 25 May 2018 | Accepted: 26 June 2018

International Journal of Dermatology 2018, **57**, 1165–1172

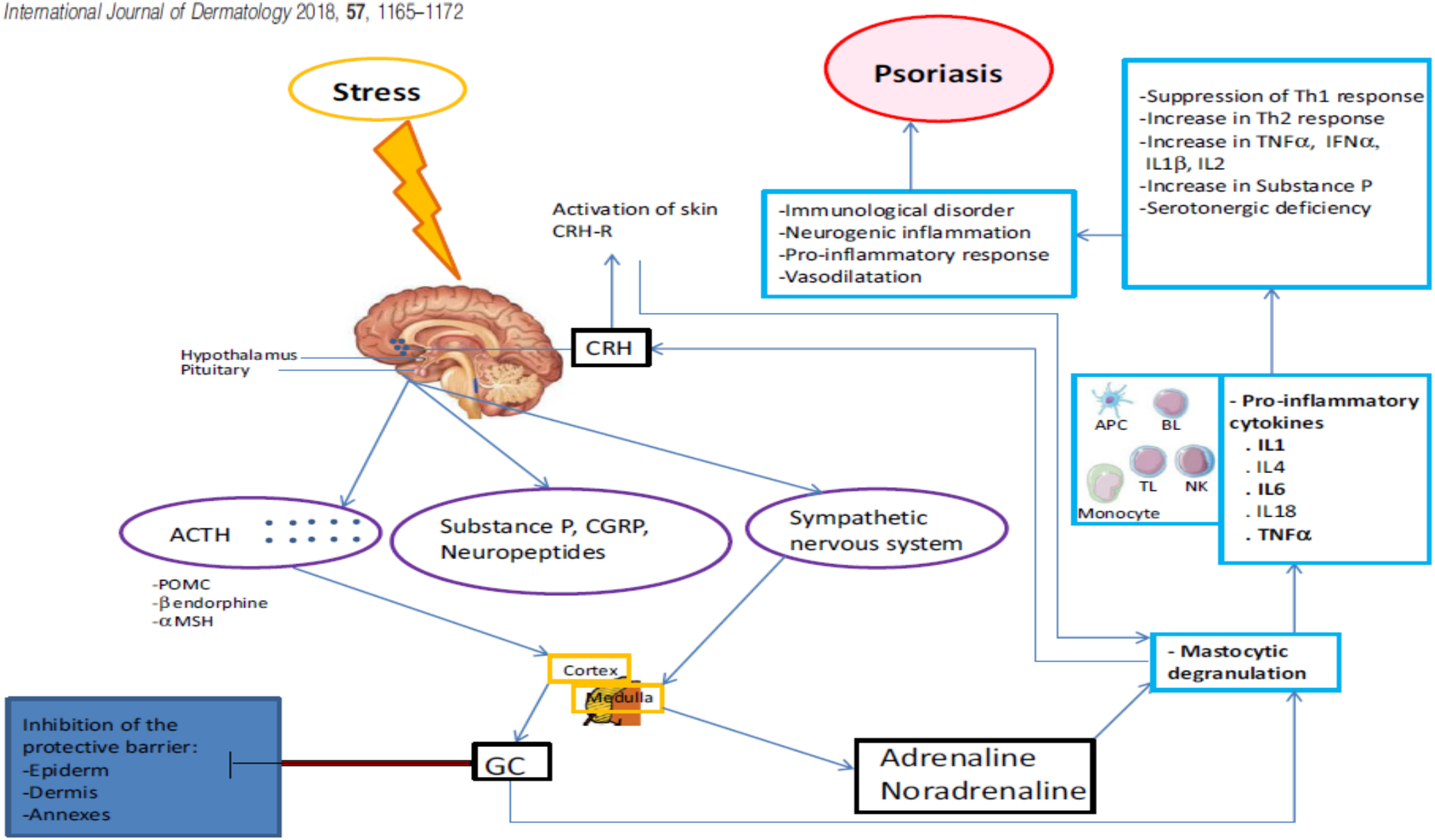


Figure 1 Physiopathology of the relationship between stress and psoriasis. CRH-R, corticotropin-releasing hormone receptor; ACTH, adrenocorticotropic hormone; POMC, proopiomelanocortin; α MSH, α Melanocyte stimulating hormone; GC, Glucocorticoid; CGRP, Calcitonine gene-related peptide