Rationale…non solo scientifico…

- Il DC è condizione di **quotidiano riscontro** nello specifico setting del MMG
- I MMG costituiscono il **1° riferimento** per i pazienti con DC, indipendentemente dall'eziopatogenesi (per una risposta assistenziale iniziale al loro problema, per essere indirizzati a Centri specialistici di TDD)
- E' purtroppo **realtà molto frequente**, a 10 anni dalla **L.38**, la carente **conoscenza e comunicazione**, **bidirezionale e complementare**, tra la **realtà del MMG e quella degli specialisti del dolore**→
- **mancata o scarsa risposta antalgica→ scadimento bio-psico-sociale e della Q.o.L. del pz→ aumento dell'impatto socio-economico del DC.**

Conclusioni 2

- A nostra conoscenza questo è il **primo contributo congiunto** tra MMG e Terapisti del Dolore
- La limitata casistica, unitamente ai favorevoli risultati raggiunti, sono **stimolo per poter ampliare questa sinergia «pilota» nello specifico setting del MMG**
- Ciò potrà avvenire solo **continuando a condividere sempre più le nostre realtà**, rendendo possibile una **attuazione concreta di quanto postulato dalla Legge 38/2010**

Grazie pirro

Grazie marrocco

PERCORSI SIMPESV PER UN AMBULATORIO DEGLI STILI DI VITA. IL DOLORE E L'ALIMENTAZIONE

Il dolore cronico nell'anziano

Maurizio Evangelista
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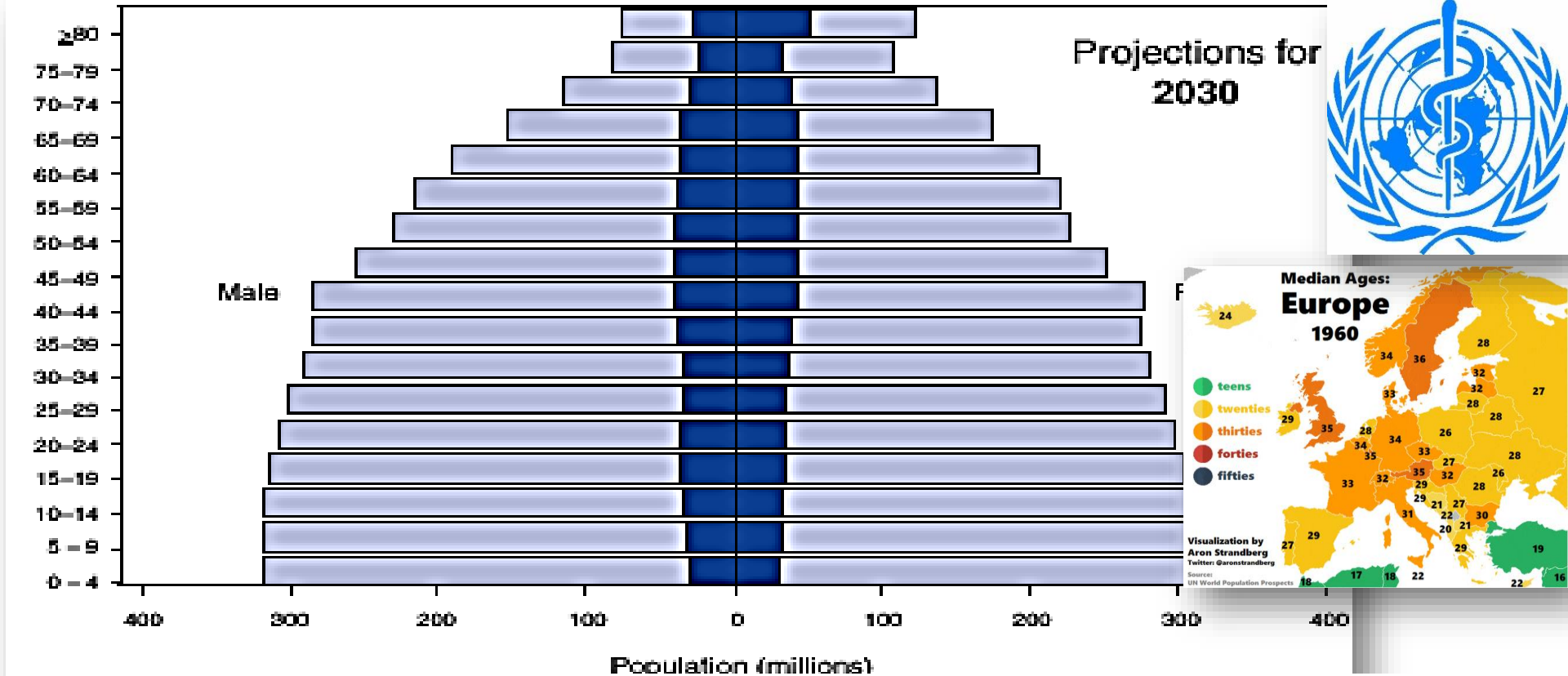
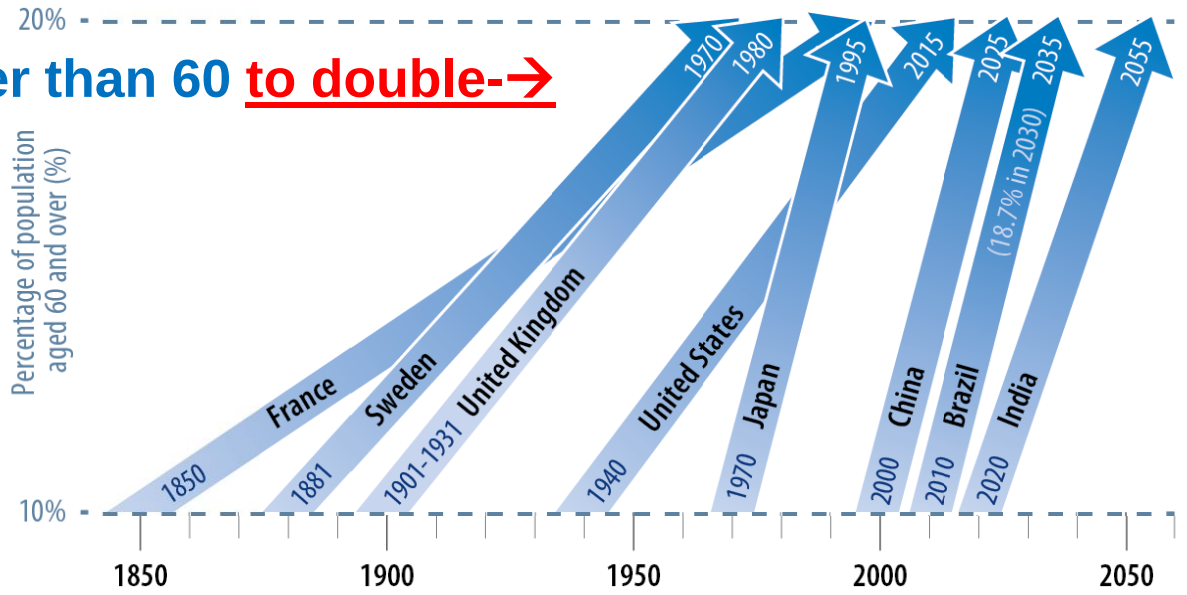
Università Cattolica del Sacro Cuore/CIC

World report on ageing and health

1. **Le Caratteristiche della Complessità Geriatrica**
2. Il dolore (cronico)
3. Le strategie per un'adeguato protocollo

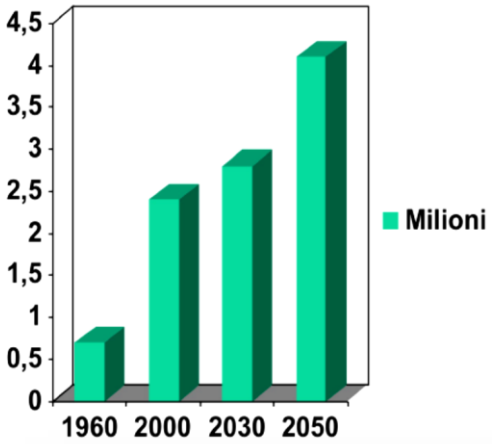


Time for % of population **older than 60 to double-→**

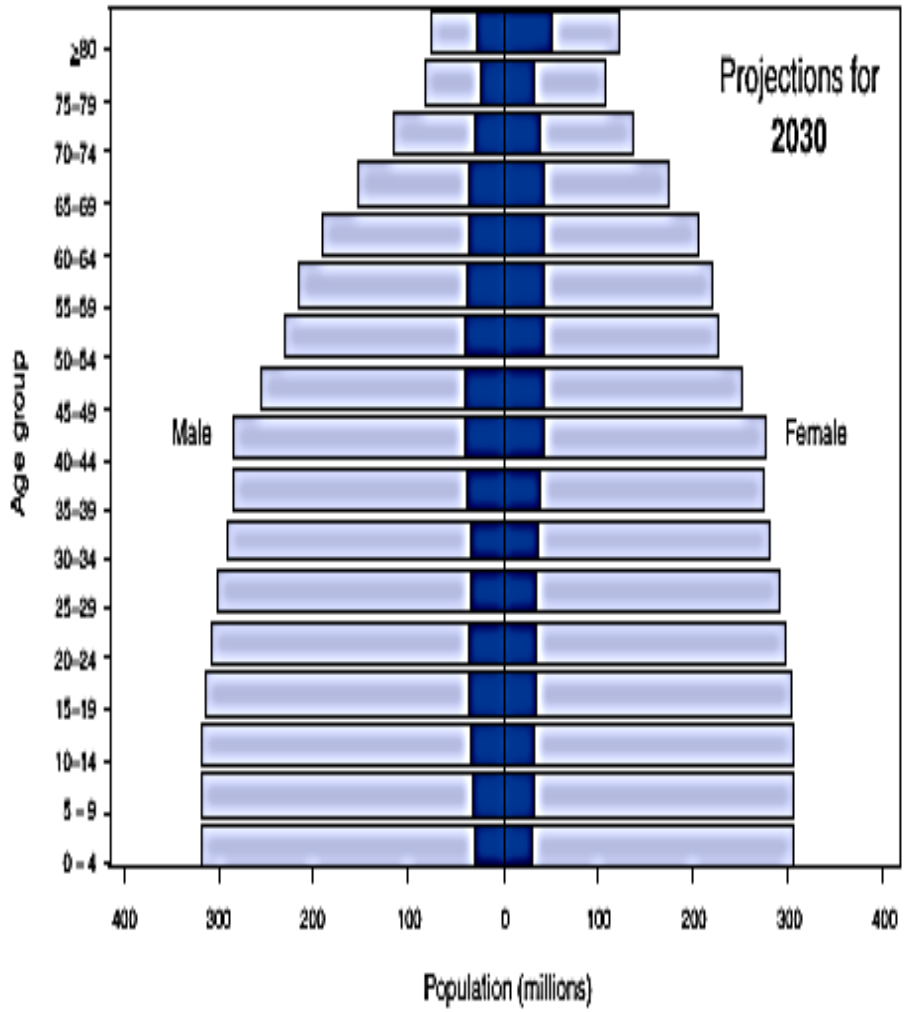


Population ageing is happening much more quickly than in the past

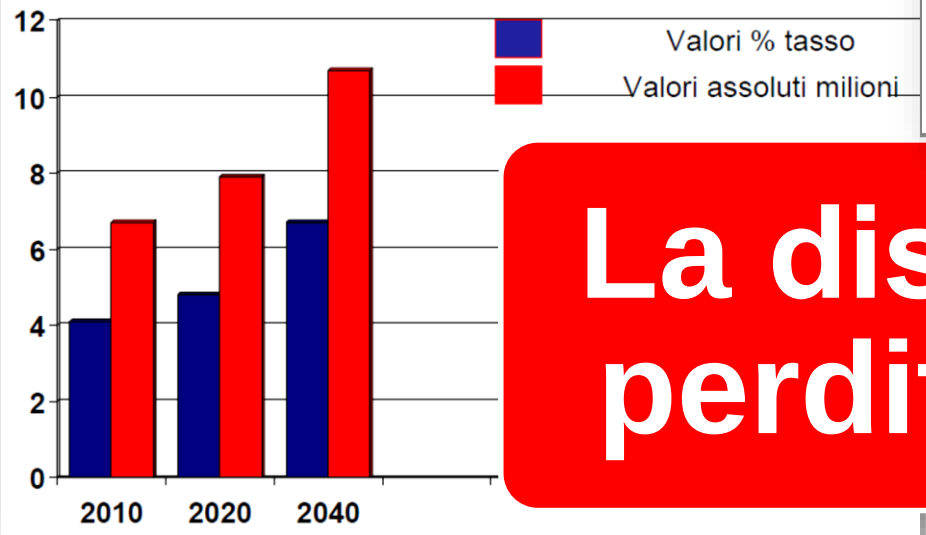
Popolazione anziana in Italia (Ultraottantenni)



1960	724.000
2000	2.476.000
2030	2.890.000
2050	4.180.000



La progressione della disabilità. Stima CENSIS 2010 – 2020 - 2040



La disabilita' indica perdita di funzione

Fragilità

Sindrome biologica e clinica caratterizzata da riduzione delle riserve e della resistenza agli stress,

provocata dal declino cumulativo di più sistemi fisiologici, in conseguenza di fattori biologici, psicologici, sociali.

Prevalenza della fragilità in Italia

65-74 a.
7%

75-84 a.
17.5 %

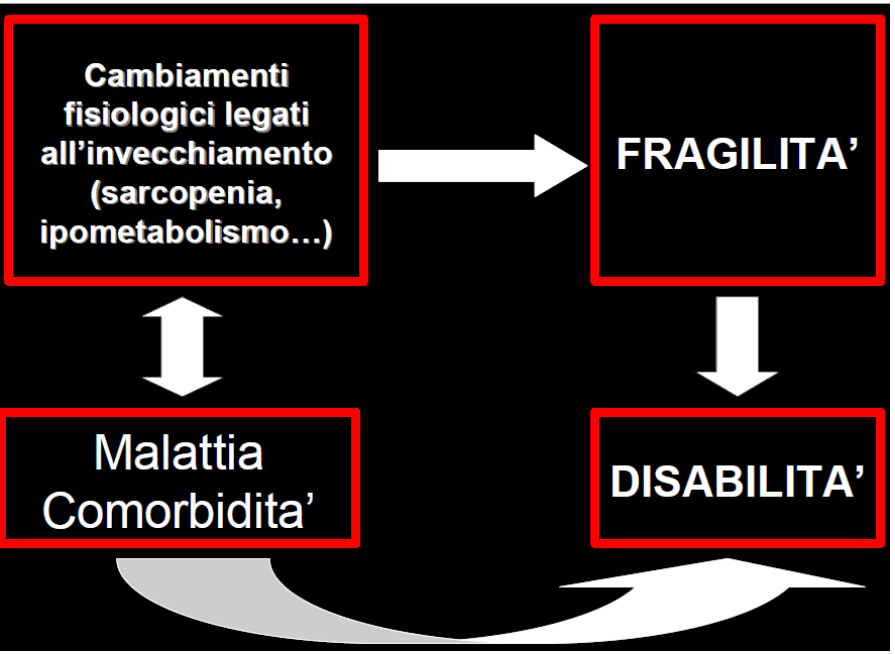
85 e +
36.6 %

Disabilità e Fragilità

≠

La disabilita' indica perdita di funzione mentre la fragilita' indica uno stato di instabilita' e di rischio di perdita o di ulteriore perdita di funzione

FRAGILITA' E DISABILITA'



ClinicalFrailty Scale		
Very fit: robusto, attivo.	Well: senza mm. attive	
Well: con mm. croniche controllate	Apparently vulnerable: con m. croniche che lo rallentano	Midly frail: dipendente in parte delle IADL
Moderately frail: con necessità di aiuto in IADL e ADL	**Severely ill: completamente dipendente o terminale**	**Canadian Study of Health and Aging**

Il fenotipo clinico-multidimensionale della fragilità sec. Rockwood

Elevata suscettibilità per mm. acute con presentazione atipica (delirium, instabilità posturale, cadute, immobilità, disidratazione)

Ridotta capacità motoria o immobilità

Fluttuazioni cliniche rapide con complicanze ("scompenso a cascata")

Rischio iatrogeno e di eventi avversi

Lenta/parziale capacità di recupero

Ripetute ospedalizzazioni, necessità di assistenza continuativa

The available literature suggests that <u>older pts have a higher prevalence of CP</u> vs younger pts.

BJA
mevg@2019

British Journal of Anaesthesia, xxx (xxx): xxx (xxxx)
doi: 10.1016/j.bja.2019.03.023
Advance Access Publication Date: xxx
Special Article

SPECIAL ARTICLE

Chronic pain: a review of its epidemiology and associated factors in population-based studies

- **<u>Advanced age and CP (and its reporting) have a complex interrelationship</u>**, whereby **<u>multi-morbidity is independently associated with CP.</u>**
- **With increasing age comes→ increasing multi-morbidity**; the more advanced a pt's age, the >likely to have experienced noxious stimuli or injury that can trigger CP.→
- → in people with shingles, those aged 50-54 yr have an 8% chance of developing PHN, **<u>whereas those aged 80-84 yr have a 21% chance of its development</u>**.

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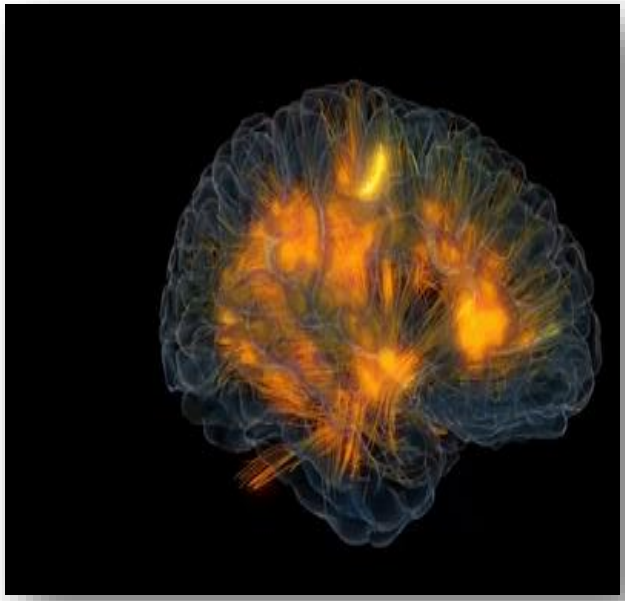
British Journal of Anaesthesia, xxx (xxxx): xxx (xxxx)
doi: 10.1016/j.bja.2019.03.023
Advance Access Publication Date: xxx
Special Article

SPECIAL ARTICLE

Chronic pain: a review of its epidemiology and associated factors in population-based studies

- **Assessing pain in older pts can be complex, particularly because older adults are often reticent to discuss or disclose the level of their pain.**
- Age related disease processes, such as cognitive decline and dementia, **can make identifying and managing** CP **more difficult.→**



Paziente che comunica

Paziente che non comunica

Self r orting

Lamenti verbali, Vocalizzazioni «negative», sospiri, gemiti,

Agitazione, pianto, smorfie, movimento/irrequietezza,

sfregamento, forza, rinforzo, rigidità, vagabondaggio, eloquio inappropriato ed aggressività

Sintomi comportamentali e psicologici di <u>demenza</u>

o di **<u>esigenze insoddisfatte quale il dolore?</u>**

- **La prevalenza del dolore** negli anziani che vivono nelle **strutture socio-sanitarie** residenziali è **marcatamente >** di quella dei coetanei che vivono in **comunità**.
- La gestione del dolore nell'anziano è tuttora ardua per numerose problematiche irrisolte:

1. ***difficoltà di diagnosi***
2. ***sostanziale carenza di studi clinici***
3. ***insufficienza di terapie efficaci e sicure***

Ne deriva che spesso il dolore degli anziani non è né ben riconosciuto né, tam poco, adeguatamente trattato. Eppure→


BJA
mevg@2019
SPECIAL ARTICLE
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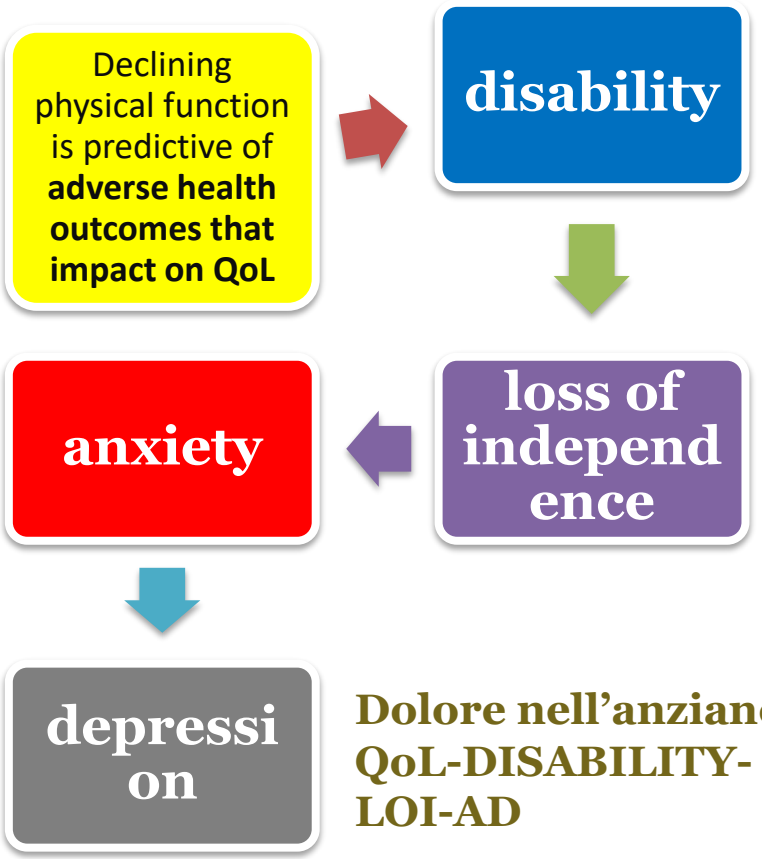
Special Article

Il dolore è tra i motivi che più frequentemente inducono il pz anziano a rivolgersi al MMG

- **La causa** non sembra essere solo l'aumentata prevalenza del dolore per l'aumentata età, **ma**
- **un aumento del dolore** ***associato a disabilità, malattie croniche, fragilità, cadute*** **ed altri problemi dell'invecchiamento…**



Dolore nell'anziano: QoL-DISABILITY-LOI-AD

1. Hasselstrom J, Liu-Palmgren J, Rasjo- Wraak G. Prevalence of pain in general practice. Eur J Pain. 2002; 6(5): 375-85.

3. Molton IR, Terrill AL. Overview of persistent pain in older adults. Am Psychol. 2014; 69(2): 197-207.

4. American Geriatrics Society Panel on the Pharmacological Management of Persistent Pain in Older Persons. Pharmacological management of persistent pain in older persons. J Am Geriatr Soc. 2009; 57(8): 1331-46.

5. Morrissey MB, Viola D, Shi Q. Relationship between pain and chronic illness among seriously ill older adults: expanding role for palliative social work. J Soc Work End Life Palliat Care. 2014; 10(1): 8-33.

Multiple sites and causes of pain

- **Characteristics of pain**, including duration and severity, area of body affected, and # of sites of pain, were found to be **indicators for ongoing pain in older women**, but these were < relevant in older men.
- **It is rare the older adult who has 1 one site of pain.**
- Pain has been reported in **multiple sites >28<59% of older adults** with women reporting greater # of pain sites . →**The # of pain sites magnifies the overall effect of pain**.
- Moreover, **older (vs younger) adults are >likely to report pain at multiple sites with > than 1 mechanism** (nociceptive, inflammatory, neuropathic) **often requiring > than 1 type of pain medication for optimal treatment**.

Il dolore è tra i motivi che più frequentemente inducono il pz anziano a rivolgersi al MMG

- **Nei Paesi industrializzati** già negli adulti **>50aa è documentata una correlazione diretta tra dolore e malattie croniche e tra dolore e multimorbidità.**
- **Queste associazioni aumentano col tempo e, tra gli anziani, >66% sono affetti da malattie croniche multiple**

1. Hasselstrom J, Liu-Palmgren J, Rasjo- Wraak G. Prevalence of pain in general practice. Eur J Pain. 2002; 6(5): 375-85.

3. Molton IR, Terrill AL. Overview of persistent pain in older adults. Am Psychol. 2014; 69(2): 197-207.

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5. Morrissey MB, Viola D, Shi Q. Relationship between pain and chronic illness among seriously ill older adults: expanding role for palliative social work. J Soc Work End Life Palliat Care. 2014; 10(1): 8-33.

Clinical:*Multi-morbidity and mortality*

Pts with **co-morbid physical and mental chronic diseases** are **> liable to suffer CP**

VS those without.

>88% of those with CP have additional chronic diagnoses.

there is an increased co-occurrence of CP with depression and CV disease.

Approximately a 1/3 of pts with

chronic pulmonary disease and coronary heart disease *report experiencing CP.*

The presence of co-morbidities also complicates the clinical management of people with CP by

limiting the applicability of disease-specific clinical GL and reducing the treatment options available for optimal pain control

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Clinical:Multi-morbidity and mortality

In people with other medical co-morbidities,

CP is an independent risk factor for all-cause mortality.

Pts diagnosed with

severe CP are 2X as likely to have died 10 yr later from ischaemic heart disease or respiratory disease

VS those who report mild CP or were pain free.

Those who were ***'resilient to pain'*** people who experienced a high pain intensity, but documented a low pain disability had an **improved 10 yr survival rate**

VS who were not resilient to pain.

Clinical:Multi-morbidity and mortality

- In pts with chronic obstructive pulmonary disease **(COPD), CP is common**, and those **with COPD+ CP were found to *have > depression, do < physical exercise*, *and have higher breathlessness scores*** than **those without COPD**.
- For those living **with neurological conditions**, the **prevalence of CP is X2** that of the general population, and those with **spinal cord injury have the highest levels of pain**.

Pain and comorbidity in older people EPIDEMIOLOGICAL STUDIES…

- …have estimated that ***approximately 20%*** **of people in this age group are** ***taking analgesic medicines*** and the majority are using these medications for **> *than 6 months' duration***.
- A survey of **> 17 000 Australian** adults found that the **prevalence of CP peaked in the range 65–69 yy for men** and 80–84 yy for women and **people > 85 yy were <likely to receive analgesia than younger subjects.**
- Older people also have the **highest rate of surgical procedures** and are >likely to suffer from MS pain and other chronic conditions VS their younger counterparts.

Pain and comorbidity in older people
CLINICAL IMPACT 1

One of the most challenging statistics is that *> 45% < 80%* of older people with pain report that

it is inadequately treated.

An observational study of 3046 community-dwelling frail older people in **Italy** found that **40% reported daily pain** but **only ¼** of these people **received analgesia**..

Pain and comorbidity in older people
CLINICAL IMPACT 2

The **clinical impact** of this is highlighted by the growing body of evidence that reveals an

association between poorly controlled pain and declining physical function in older people.

A large longitudinal study of community-dwelling people > 70 (*n* = 754) demonstrated a

significant association between the incidence of restrictive back pain and reduction in lower limb function.

Similarly, a study examining the **relationship between daily pain and physical function in the oldest old** (mean age 85) found that

those reporting daily pain had significantly lower scores in a physical performance battery and lower grip strength.

Pain in Neurodegenerative Disease: Current Knowledge and Future Perspectives.1

- *Neurodegenerative diseases are* ***going to increase as the life expectancy is getting longer.***
- ***The management of NDD*** such as **Alzheimer's disease** (AD) and **other dementias**, **Parkinson's disease** (PD) and PD related disorders, **motor neuron diseases** (MND), **Huntington's disease** (HD), **spinocerebellar ataxia** (SCA), and **spinal muscular atrophy** (SMA), is ***mainly addressed to motor and cognitive impairment***, with special care to vital functions as breathing and feeding.
- **Many of these patients complain of painful symptoms *and their presence is frequently not considered in the treatment GL***, leaving their management to ***the decision of the clinicians alone.***

Pain in Neurodegenerative Disease: Current Knowledge and Future Perspectives2

- However, studies focusing on pain frequency in such disorders suggest a high prevalence of pain in selected populations
- **from 38 to 75% in AD**
- **40% to 86% in PD**
- and **19 to 85% in MND**.
- The **methods of pain assessment vary** between studies so **the type of pain has been rarely reported.**
- However, **a prevalent non neuropathic origin of pain emerged for MND and PD**. In **AD, no data on pain features are available**.
- **No controlled therapeutic trials and GL are currently available**.
- Given the relevance of pain in NDD disorders, the comprehensive understanding of mechanisms and predisposing factors, the application and validation of specific scales, and new specific therapeutic trials are **needed.**

Clinical:Mental health

Because of the bidirectional relationship between CP and mental health conditions,

screening for mental health issues in people with CP,

and for CP in people with mental health issues,

should be considered

Pain-Sleep Connection

When sleep deprived...

↓ Frontal Lobe

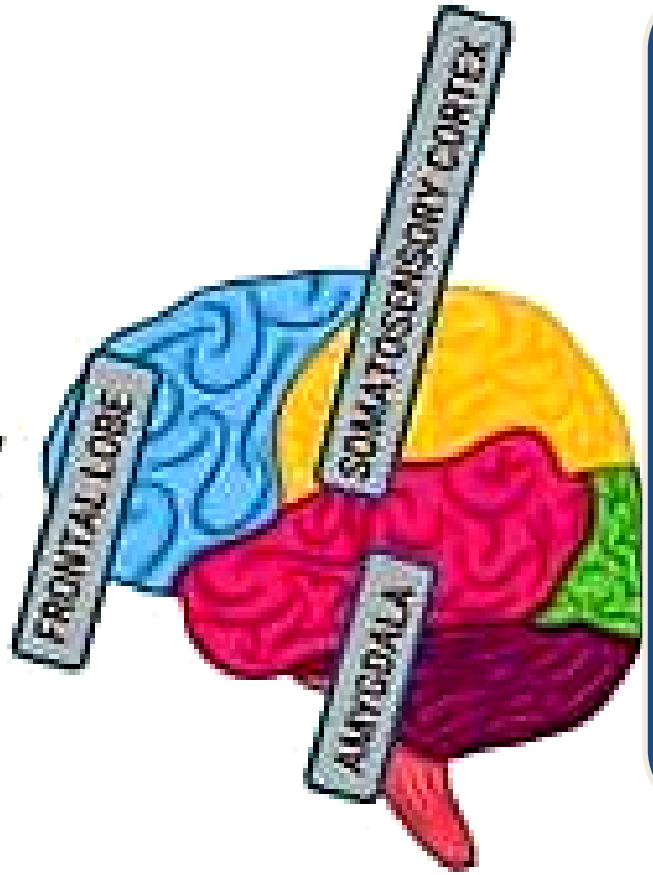
Decreased decision making and problem solving abilities

↑ Somatosensory Cortex

increased reactivity to stimuli (including nociceptors)

↑ Amygdala

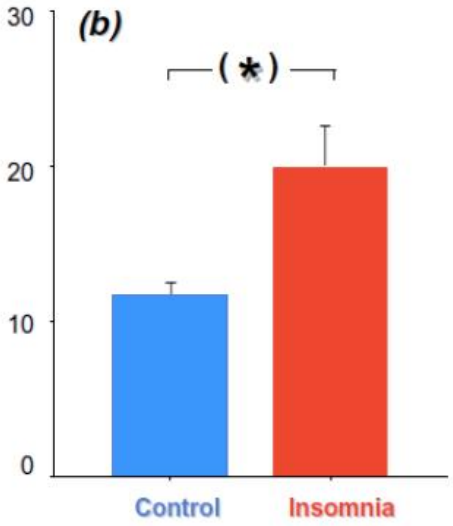
increased perception of fear and other emotions



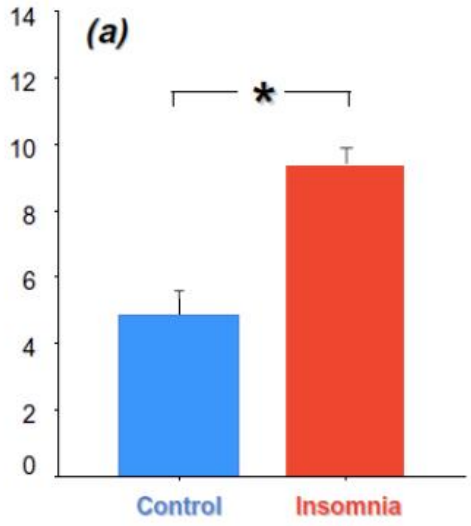
The association is bidirectional, with CP causing poor sleep, and poor sleep increasing the intensity and duration of CP.

Worsened Sleep = Worsened Pain

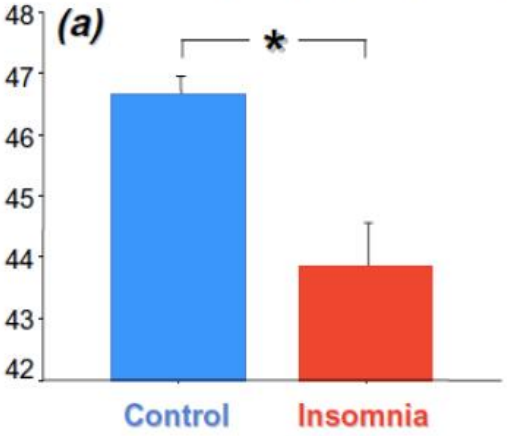
Pain Intensity (units)



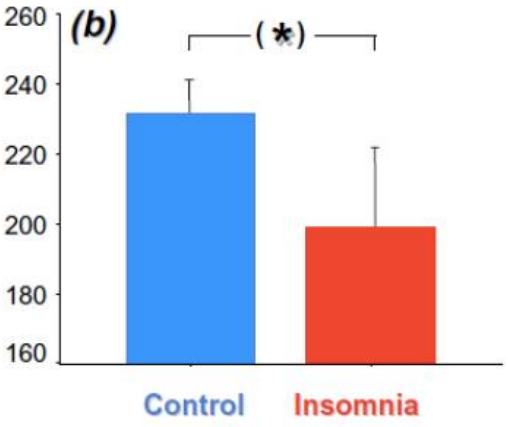
Pain Frequency (number of days out of 14 days)



Heat Pain Threshold (HPTh, °C)



Pressure Pain Threshold (PPTh, kPa)



Haack M., et al. Eur J Pain 2012

Clinical: Sleep disorders

- Sleep disorders have been shown to **affect nearly 50% of people reporting CP**, with a 25% of CP pts suffering from clinical insomnia.
- ***The association is bidirectional, with CP causing poor sleep, and poor sleep increasing the intensity and duration of CP.***
- Sleep deprivation was found to be a risk factor for CP in a prospective survey of **women over a 17 yr period.**

- There is a **high prevalence of sleep apnoea in pts who take opioid medications long term**, but **pts with CP are at higher risk of developing sleep apnoea irrespective of opioid medication**

Clinical: Sleep disorders

- **Another study showed that having CP made people >likely to suffer from sleep problems and depression, and suggested that *treating sleep disorders should be considered as part of CP management.***

Neuropsychopharmacology
Neuropsychopharmacology (2019) 0:1–12;
https://doi.org/10.1038/s41386-019-0439-z
www.nature.com/npp

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NEUROPSYCHOPHARMACOLOGY REVIEWS

Sleep deficiency and chronic pain: potential underlying mechanisms and clinical implications

Impact of Persistent Pain: Sleep, Activity, and Mood 1

- In a state of persistent pain, **older adults may limit what they do, either because activity exacerbates the pain or because they are afraid of reinjury or falling**.
- **Limiting physical activity because of pain is a natural strategy for certain acute pain** conditions in which pain results from an injury that requires rest to heal.

Impact of Persistent Pain: Sleep, Activity, and Mood 1BIS

- However, in the case of persistent pain, **limiting activity may lead to a cycle of restriction, decreased participation, and greater disability**
- Aside from a **reduction in social engagement and meaningful activities**, **a decline in physical activity because of pain is also associated with weight gain and obesity**, which **can contribute to even greater pain**, especially in the **knees, hips, and lower back**

Impact of Persistent Pain: Sleep, Activity, and Mood2

- Persistent pain **may also lead to chronic problems in initiating and maintaining sleep**.
- Older adults with severe, persistent pain are **2X** as likely to **report difficulties in initiating sleep, in staying asleep, and with sleeping longer than usual**.
- **This is especially the case for individuals who have pain at multiple sites** (***as older adults frequently do***) and is true even after controlling for comorbid health conditions and anxiety

Impact of Persistent Pain: Sleep, Activity, and Mood 2BIS

Consequently, as many as 42% of middle-aged and older adults with persistent pain **experience chronic sleep deprivation**

since **poor sleep leads to persistent fatigue in older adults** and **fatigue leads to decreases in physical activity and to greater disability**

The relationship between pain-related sleep deprivation and physical inactivity may also be critical,

World report on ageing and health

Le Caratteristiche Della Complessità Geriatrica

- Niente è stabile per lungo tempo
- I domini compromessi sono molteplici
- L'ambiente è una dimensione centrale
- Gli operatori sono interdipendenti
- I dati clinici sono incerti e contrastanti
- "Small gains" come risposta dell'intensività
- La necessità di "ridurre" gli interventi alla "sintesi"

World report on ageing and health

1. Le Caratteristiche Della Complessità Geriatrica
2. **Il dolore (cronico) e Le strategie per un'adeguato protocollo**

La teoria del continuum

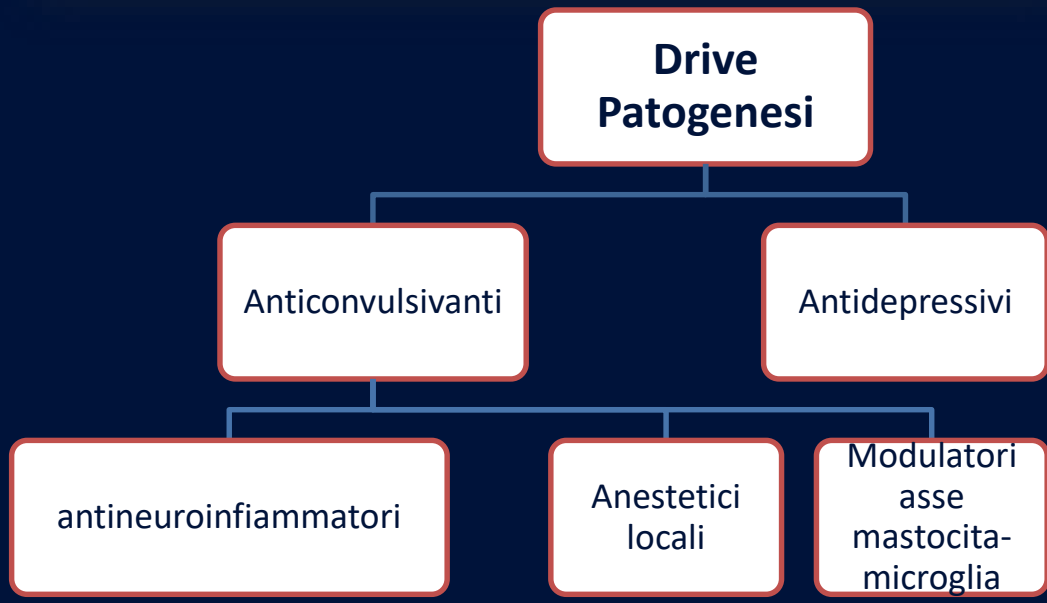
<1 mese

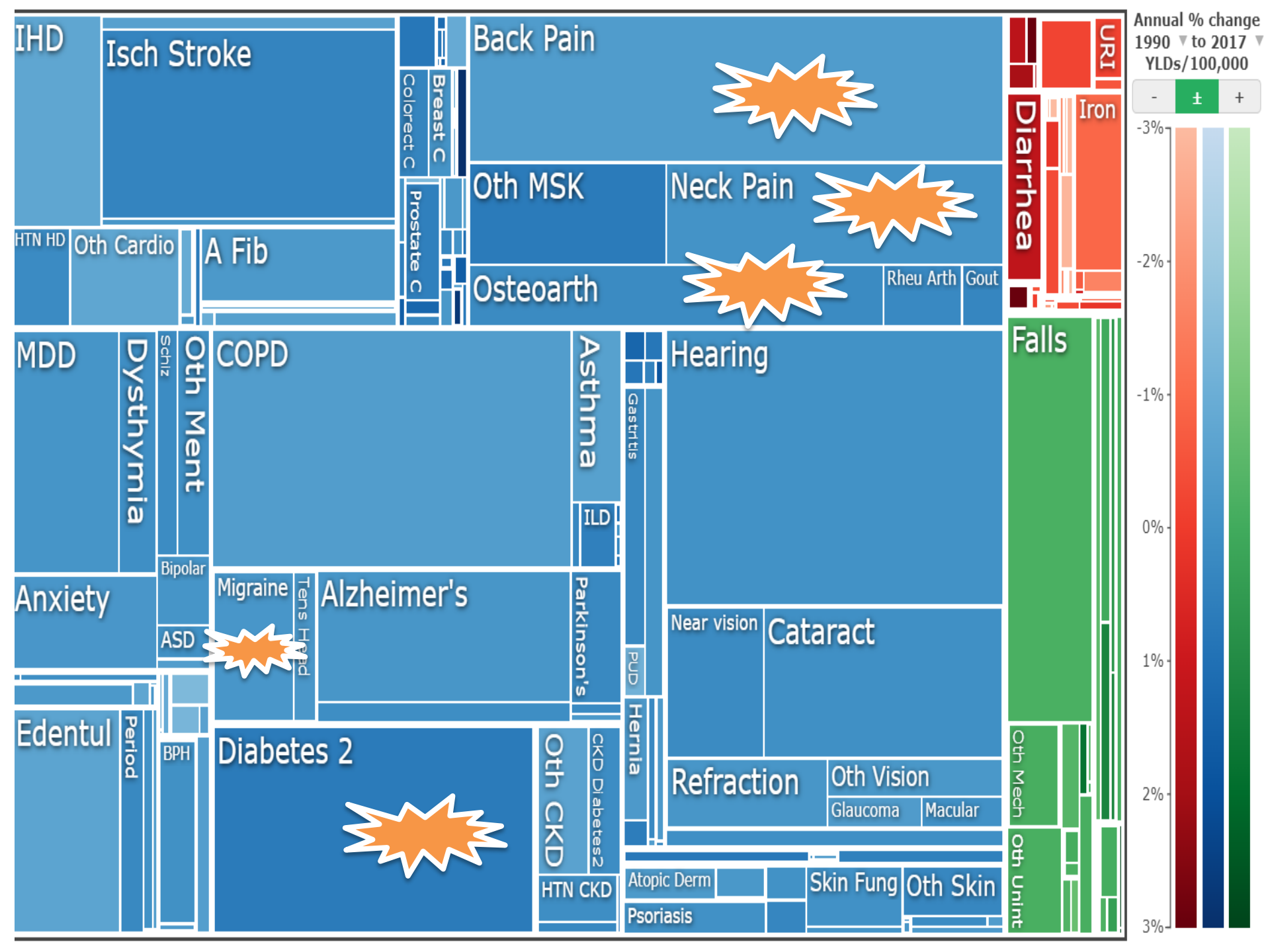
- Danno tissutale generalmente evidente
- Aumentata attività del sistema nervoso
- Dolore che si risolve dopo la guarigione
- Ha una funzione protettiva

Cole BE. Hosp Physician. 2002; 38: 23-30.
Turk and Okifuji. Bonica's Management of Pain. 2001.
Chapman and Stillman. Pain and Touch. 1996.

≥3-6 mesi

- Dolore per 3-6 mesi o più
- Dolore oltre il periodo atteso di guarigione
- In genere non ha funzione protettiva
- Peggioramento della salute e delle funzioni

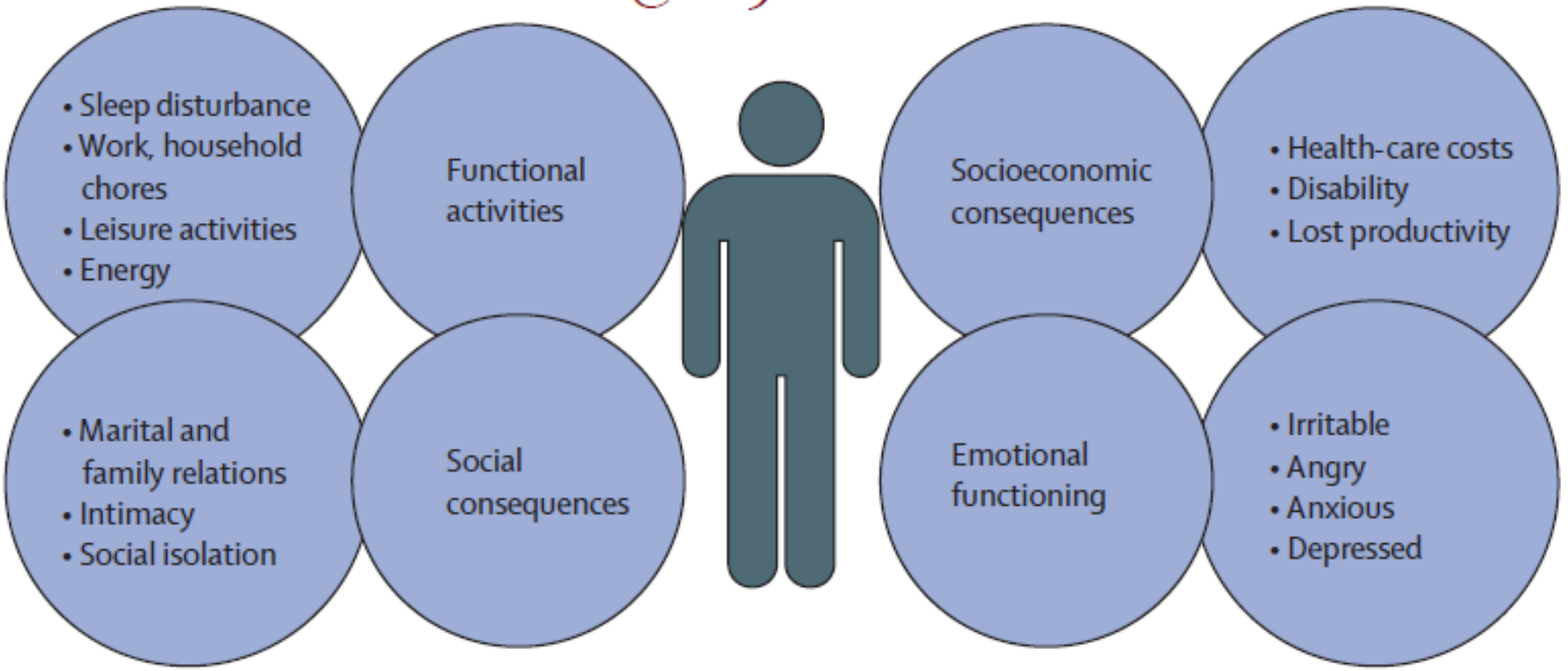



IHD
Isch Stroke
Back Pain
Coloerct C
Breast C
Prostate C
Oth MSK
Neck Pain
HTN HD
Oth Cardio
A Fib
Osteoarth
Rheu Arth
Gout
URI
Diarrhea
Iron
MDD
Dysthymia
Schiz
Oth Ment
COPD
Asthma
ILD
Gastritis
Hearing
Falls
Bipolar
Anxiety
ASD
Migraine
Tens Head
Alzheimer's
Parkinson's
PUD
Hernia
Near vision
Cataract
Refraction
Oth Vision
Glaucoma
Macular
Oth Mech
Oth Unint
Edentul
Period
BPH
Diabetes 2
Oth CKD
CKD Diabetes2
HTN CKD
Atopic Derm
Psoriasis
Skin Fung
Oth Skin
Annual % change
1990 to 2017
YLDs/100,000
-
±
+
-3%
-2%
-1%
0%
1%
2%
3%

Treatment of chronic non-cancer pain The Lancet
Prof Dennis C Turk, PhD, Hilary D Wilson, PhD, Prof Alex Cahana, MD
Volume 377, Issue 9784, Pages 2226-2235 (June 2011) DOI: 10.1016/S0140-6736(11)60402-9

«LE CONSEGUENZE» DEL DOLORE CRONICO NON ONCOLOGICO

MEVG@2019FOCUS#10



The effect and burden of chronic pain

CP affects **every aspect of a patient's life**, contributing to a **loss of both physical and emotional function**, affecting a patient's **levels of activity** (ability to work at **home** and **job** and engage in **social** and **recreational** pursuits); additionally, there are often **serious economic consequences** as a result of health-care bills and potential loss or decrease in financial income.

Pain Management in the Elderly

Monica Malec, MD[a], Joseph W. Shega, MD[b,*]

Overview of a comprehensive pain assessment

Domain	Components
Pain presence	At rest, with activity
Pain intensity	Now, on an average day, worst pain, lowest level of pain
Pain characteristics	Location, frequency, exacerbating and relieving factors, character, and natural history
Pain physiology	Nociceptive, neuropathic, or mixed
Pain interference with activity and pain-related morbidity	Physical, psychological, spiritual, and social functioning, falls, sleep, appetite, etc
Painful conditions	Osteoarthritis, osteoporosis, previous bone fractures, diabetic neuropathy, post-herpetic neuralgia, myofascial pain syndromes, etc
Pain behavior	Facial expressions, vocalizations, body movements, changes in interpersonal interactions and routines, and mental status changes
Pain treatment	Nonpharmacologic and pharmacologic including injections, surgical interventions, and alternative therapies
Coping style	Distraction, ignoring pain sensations, reinterpreting pain sensations, catastrophizing, praying, and hoping
Sensory	Hearing, vision, and cognition
Proxy report	Professional and family caregiver

Examples of pharmacokinetic changes with ageing

Drug absorption

Changes to active transport	Reduced absorption of vitamin B_{12}, iron and calcium through active transport
Reduced dopa decarboxylase in gastric mucosa	Increased absorption of levodopa

First-pass metabolism

Reduced liver mass and blood flow	Increased bioavailability of drugs with extensive first-pass metabolism (e.g. propranolol, labetalol)
	Reduced activation of pro-drugs activated in the liver (e.g. enalapril, perindopril)

Protein binding

No substantial age-related changes

Drug distribution

Relative reduction in total body water	Reduced volume of distribution and increased serum concentrations of water-soluble drugs (e.g. gentamicin, digoxin)
Relative increase in body fat	Increased volume of distribution and longer half-life of lipid-soluble drugs (e.g. diazepam, thiopental, lidocaine)

Drug clearance

Reduction in glomerular filtration rate	Reduced clearance of renally excreted drugs (e.g. water-soluble antibiotics, diuretics, digoxin, lithium)
Reduction in liver mass and blood flow	Reduced clearance of drugs with a high hepatic extraction ratio (e.g. clomethiazole, glyceryl trinitrate, lidocaine, pethidine, propranolol)

Practical advice for prescribing in old age

Key points

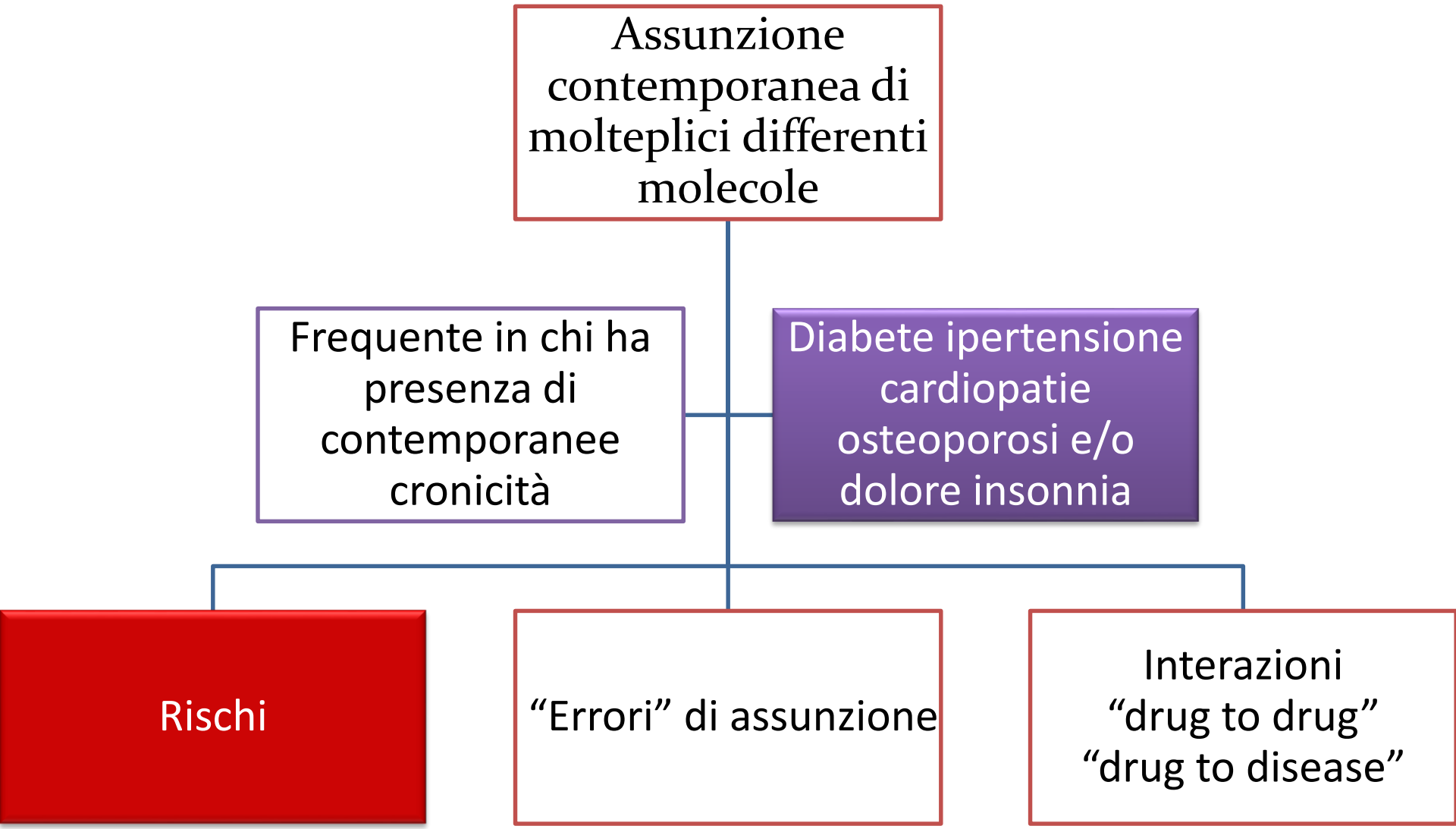
- Prescribing in the older person with frailty is different from prescribing in young, fit adults
- Careful consideration of the benefits and risks of prescribing and continuing to prescribe medications is necessary for this group
- Quality of life, rather than therapeutic efficacy, may be more important in people with short life expectancy
- Polypharmacy is of particular concern in older people who, compared with younger individuals, tend to have more disease conditions for which therapies are prescribed
- Awareness of particular medications that are often harmful in this group is essential for good practice

Effects of polypharmacy in the elderly

- Increased risk of adverse drug events due to metabolic changes and decreased drug clearance
- Increased potential for drug–drug interaction
- Increased possibility of a 'prescribing cascade' – this develops when an adverse drug event is misinterpreted as a new medical condition and additional drug therapy is prescribed to treat this perceived medical condition
- Use of multiple medications can lead to problems with adherence, compounded by visual or cognitive compromise in many older adults

JAMA Internal Medicine, 2017, 177#6:871

JAMA 7,2017, 318#17: POLIPHARMACY



JAMA 7,2017, 318#17
POLIPHARMACY

DRUG DISEASE INTERACTION

FANS

- POSSIBILE RIALZO PRESSORIO
- POSSIBILE PEGGIORAMENTO FUNZIONALITA' RENALE

POLIPHARMACY
JAMA Internal Medicine, 2017, 177#6:871

- **Molto comune**: **circa il 20% degli >65 aa. assume 10 o > medicazioni/die→nei pz che assumono 8 o > farmaci vs chi ne assume <4 il RR di eventi avversi → x4**
- >10% dei ricoveri è causato dagli eventi avversi
- **Le *"fisiologiche"modificazioni* farmacocinetiche/dinamiche associate all'età aumentano il rischio di eventi avversi**
- **La > parte delle prescrizioni è in accordo con le LG→** Il rischio di "danno" (EC, ospedalizzazioni) è nella ***mancata considerazione dell' "intero contesto" e delle circostanze specifiche del pz***

Strategie per ottimizzare la prescrizione “sicura”

- Verificare la reale necessità di una prescrizione **(la patologia è ancora in atto?)**
- Chiedere una **lista “aggiornata”** di tutte le sostanze prescritte dal proprio **MMG e dagli altri specialisti**, compresi i farmaci **“over the counter”** (ranitidina, loratadina, integratori, omeopatia).
- Coinvolgere **famiglia e “caregiver”,** specialmente per situazioni di deterioramento cognitivo
- Identificare, **in maniera bilaterale**, quali sono i sintomi o le patologie **“realmente” attive nel peggiorare la Q.o.L.**→alcune sostanze potrebbero risultare **“non indispensabili”**
- **Semplificare lo schema terapeutico (OAD, OAW)**

Strategie per ottimizzare la prescrizione “sicura”

- **La “polipharmacy” è un reale problema per il paziente anziano**
- **L’ottimizzazione di uno schema terapeutico**, in generale e nello specifico setting della TDD e della CP, **si basa sulle LG ma**
- deve tenere in conto, in egual misura,

1. le preferenze del pz e
2. le esigenze del suo specifico contesto (tailoring) nonché
3. accessibilità,
4. tollerabilità ed evitamento delle ospedalizzazioni

I punti chiave per l'approccio farmacologico e non

1. **Collegare** i benefici potenziali del trattamento con i più importanti obiettivi del paziente (esempio: una maggiore capacità di svolgere le attività della vita quotidiana)
2. **Utilizzare** le combinazioni di farmaci (**in cui ogni analgesico agisce su un diverso meccanismo***) per migliorare l'efficacia analgesica (**multimodalita, inter e multidisciplinarietà**)
3. *Il paracetamolo rimane prima linea di trattamento farmacologico per gli anziani con dolore lieve-moderato*
4. **Evitare** FANS **orali** per lungo termine (significativo rischio CV, GI e renale)
5. **l'utilizzo di oppioidi è appropriato per i pazienti non responsivi alle terapie di 1° linea** che continuano a sperimentare **significativo deterioramento funzionale a causa del dolore**

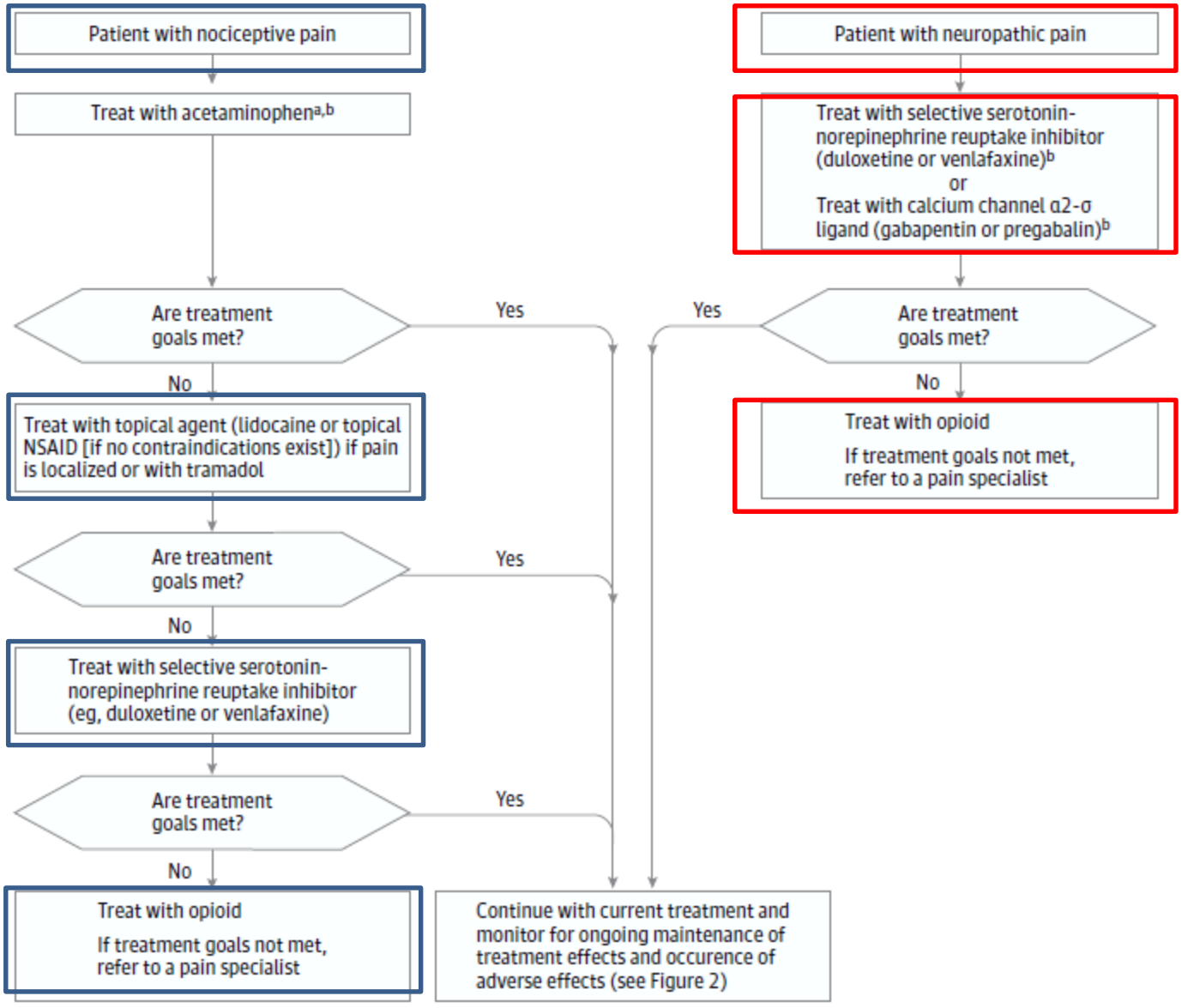
Practical advice for prescribing in old age

I punti chiave per l'approccio farmacologico e non

- 6. **Considerare** gli inibitori della ricaptazione di serotonina-norepinefrina o selettivi nei pazienti **con depressione** in comorbidità
- 7. **Implementare** piano di sorveglianza (l'efficacia, la tollerabilità, l'adesione) con ogni nuovo trattamento
- 8. **L'attività fisica** (compresa la terapia fisica, esercizio fisico, o altro) costituisce una **componente essenziale della gestione del dolore persistente** nei pazienti più anziani
- 9. **Determinare** se gli obiettivi del trattamento sono stati raggiunti; se non, i protocolli devono essere adeguati o interrotti, ed integrati con terapia fisica e terapia occupazionale

Practical advice for prescribing in old age

Figure 1. Treatment Algorithms for Nociceptive and Neuropathic Pain Disorders in Older Adults



[a] Recommend use of oral nonsteroidal anti-inflammatory drugs (NSAIDs) in appropriate patients for selected situations (eg, acute-on-chronic pain flare, brief rehabilitation period, acute injury).

[b] Consider combination therapy when possible (eg, acetaminophen + serotonin-norephinephrine reuptake inhibitor) for the treatment of nociceptive and neuropathic pain.

n engl j med 373;22 nejm.org november 26, 2015

Intensity of Chronic Pain — The Wrong Metric?

Jane C. Ballantyne, M.D., and Mark D. Sullivan, M.D., Ph.D.

NEUROCENTRICO
(stabilizzatori di membrana, potenziatori delle vv discendenti)

ANTICONVULSIVANTI
ANTIDEPRESSIVI ANESTETICI LOCALI*

ANTINFIAMMATORIO
fans os\patch curcumina

MODULATORI DI MICROGLIA E MASTOCITA

POPOLAZIONI NON NEURONALI
PEA (polidatina, luteolina,

(tramadolo buprenorfina patch)

ORIENTATO AL MECCANISMO: multiple molecole per multipli meccanismi

Lg IASP

Lg EFSN

Specific Pharmacologic Agents

BJCP British Journal of Clinical Pharmacology

Clinical pharmacology of analgesic medicines in older people: impact of frailty and cognitive impairment

Topicals

Transdermal

Acetaminophen

Nonsteroidal antiinflammatory drugs

"Adjuvant Therapies"

Antidepressant

Antiepileptics

CONTINUING MEDICAL EDUCATION

The Pharmacological Therapy of Chronic Neuropathic Pain

2016

Andreas Binder, Ralf Baron

BOX 2

Realistic goals for the treatment of neuropathic pain

- Reduction of pain by > 30–50%
- Improved sleep
- Improved quality of life
- Maintenance of social activities and relationships
- Recovery and maintenance of the ability to work

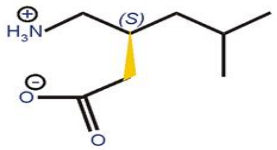
The pharmacotherapy of neuropathic pain: number of trials, number of patients, number needed to treat, evidence levels (GRADE [27]), and common side effects (modified from [6])

	Number of trials	Number of patients	Number needed to treat [95% CI]	Evidence level (GRADE)	Examples of common side effects (may vary depending on drug and manufacturer)
Tricyclic antidepressants	15	948	3.6 [3.0; 4.4]	High	Drowsiness, fatigue, dizziness, hypotension, weight gain
Serotonin-norepinephrine reuptake inhibitors	10	2541	6.4 [5.2; 8.4]	High	Nausea, dry mouth, somnolence, headache
Pregabalin	25	5940	7.7 [6.5; 9.4]	High	Drowsiness, somnolence, peripheral edema, weight gain
Gabapentin	14	3503	7.2 [5.9; 9.1]	High	Somnolence, dizziness
Tramadol	6	741	4.7 [3.6; 6.7]	Intermediate	Dizziness, nausea
High-potency opioids	7	838	4.3 [3.4; 5.8]	Intermediate	Sedation, dizziness, headache, constipation, nausea, itch
Capsaicin 8% patch*	6	2073	10.6 [7.4; 18.8]	High	Pain or erythema at the site of application

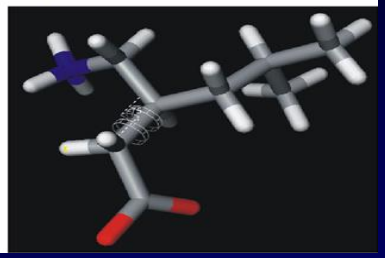
*Only peripheral neuropathic pain. CI, confidence interval. Only evidence of high or intermediate quality was considered in the construction of this table

Pregabalin: proprietà fisico-chimiche

Pregabalin
S-(+)-3-isobutilGABA



- Aminoacido
- Assorbito a livello intestinale
- Attraversa rapidamente la barriera emato-encefalica



Dosage Adjustments for Renal Impairment

Creatinine Clearance, ml/min	Maximum Daily Pregabalin Dose, mg	Maximum Daily Gabapentin Dose, mg
≥60	600	3,600
30–60	300	1,400
15–30	150	700
15	75	300

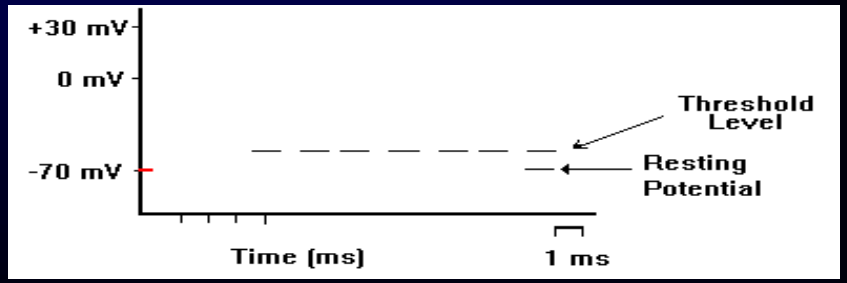
Pregabalin: indicazioni terapeutiche approvate

- ***Dolore neuropatico***: periferico e centrale negli adulti.
- ***Epilessia***: come terapia aggiuntiva negli adulti con attacchi epilettici parziali in presenza o assenza di generalizzazione secondaria.
- ***Disturbo d'ansia generalizzata***: (GAD) negli adulti.
- ***Fibromialgia***: *al momento solo in USA e Canada (FDA).*

Pregabalin **si lega alle subunità α_2-δ dei canali del calcio voltaggio dipendenti**

Pregabalin **modula l'ingresso di ioni calcio a livello delle terminazioni pre-sinaptichenei neuroni iperattivati**

Pregabalin **riduce il rilascio dei neurotrasmettitori eccitatori** (es. glutammato, sostanza P, noradrenalina)



Pregabalin: favorevole profilo farmacocinetico (I)

Variabile	Pregabalin	Rilevanza Clinica
Assorbimento	T_{max} ≤1 ora	Rapido raggiungimento dei livelli plasmatici. Somministrazione con o senza cibo
Biodisponibilità	≥90%	Indipendenza dalla dose
Farmacocinetica (150-600 mg/die)	Lineare Dose-proporzionale	Chiara relazione dose-risposta
Emivita plasmatica	6,3 ore	Posologia suddivisibile in due somministrazioni

Pregabalin: favorevole profilo farmacocinetico (II)

Variabile	Pregabalin	Rilevanza Clinica
Steady state	24-48 ore	Rapido potenziale di adattamento posologico
Legame proteico	Assente	Nessuna potenziale interazione farmacocinetica con altri farmaci
Metabolismo epatico	Irrilevante (<2%)	Non induce o inibisce gli enzimi epatici
Escrezione renale	98% come farmaco immodificato	Nessuna correzione posologica nei pazienti epatopatici

Pregabalin: assenza di interazioni farmacocinetiche clinicamente rilevanti

CLASSI FARMACOLOGICHE	
Coxib / Fans	*Insulina / Antidiabetici orali* *
Cortisonici	*Antibiotici*
Miorilassanti	*Contraccettivi orali*
Oppioidi *	*Anticoagulanti* *
Antidepressivi *	*Antiaggreganti* *
Alendronati / Difosfonati *	*Antipertensivi* *

Differenze tra pregabalin e gabapentin

	Pregabalin	Gabapentin
Assorbimento	**Non-saturabile nel range terapeutico**	**Saturabile**
Biodisponibilità	**≥ 90%**	**≤ 50%**
Dosaggio giornaliero	**BID/TID**	**TID**

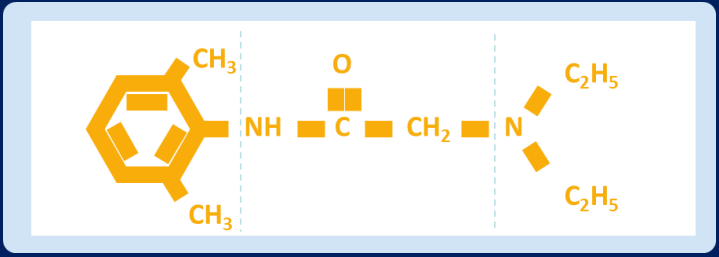
Lidocaina cerotto 5% Applicazione Topica

Differenze tra somministrazione topica e transdermica

Somministrazione transdermica

Assorbimento e azione sistemica di una sostanza

Possibili interazioni farmacologiche ed effetti collaterali sistemici



Somministrazione topica

- Azione locale al sito di applicazione
- Efficacia non legata all'assorbimento sistemico
- Bassa concentrazione sierica del farmaco

Riduzione delle interazioni farmacologiche e degli effetti collaterali sistemici

Consequences for potential predictors

Probability of Success	Potential Predictors	Long term use (months-years)	Short term use (days-weeks)
HIGH (Higher if an indication is combined with a green predictor)	Localized ■ Allodynia ■ Burning ■ Stabbing ■ Shooting ■ NRS score	■PHN ■DPN ■Trigeminal neuralgia ■Chronic post-surgical ■CRPS	■Scar pain (post surgery) ■Post Herpes Zoster
MEDIUM (Higher if an indication is combined with a green predictor)	■ Hyperalgesia	■Low Back pain (chronic) ■(Cancer pain)	■Low back pain ■Carpal tunnel syndrome ■(Fractures)
LOW / NO (lower if an indication is combined with a red predictor)	■Deep pain ■Numbness ■Radiating pain ■Radicular pain ■Heavy sweating ■Pain site distant from nerve damage ■Chronic widespread	■Central Pain	■Fibromyalgia ■Arthrosis ■Gout ■Phantom limb pain ■Muscular pain

Adapted from IEPP feedback, Vienna 2009

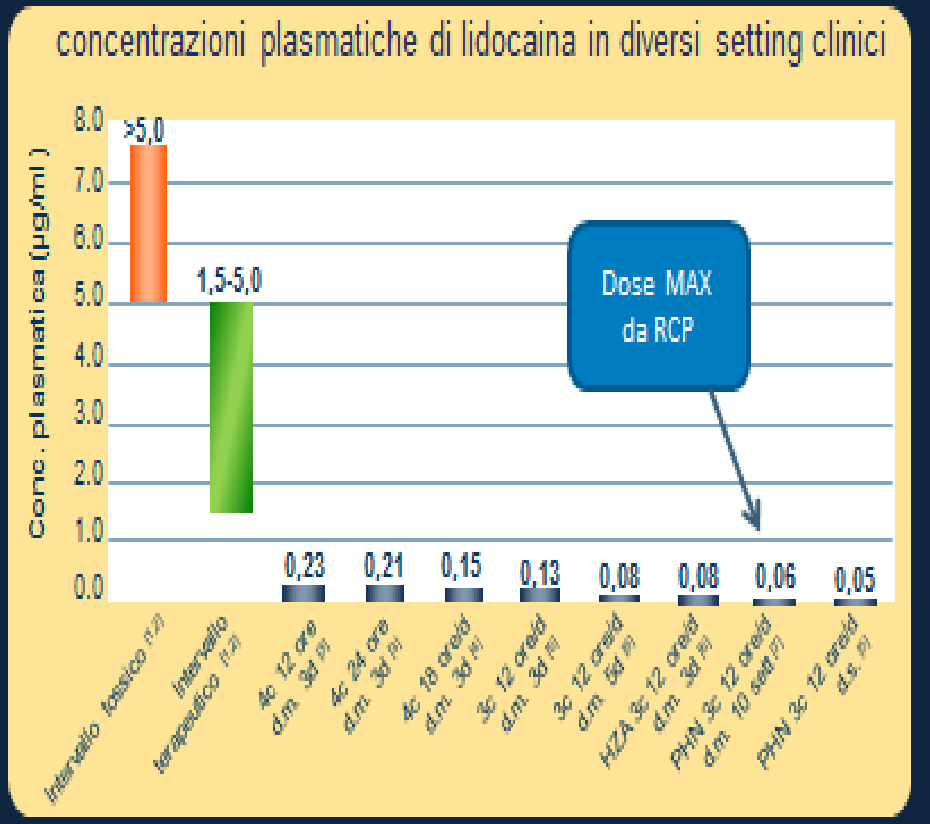
Lidocaina cerotto 5%
Assorbimento e concentrazioni plasmatiche

Gammaitoni AR and Davies MW. Ann Pharmacother 2002; 36:236-40.
Campbell BJ et al. J Pharm Sci 2002; 91:1343-50.

- Utilizzo del cerotto medicato secondo la massima dose raccomandata

  → assorbimento di **circa 3 ± 2%** della dose totale di lidocaina applicata

  → concentrazioni ematiche **clinicamente non rilevanti**



c=cerotto; d.m.=dose multiple; d.s.=dose singola HZA=Herpes zoster acuto; PHN=Nevralgia post-erpetica

1. **La manifestazione di reazioni avverse sistemiche è improbabile**
2. **Basso rischio di interazioni farmacologiche**

Key Messagges Efficace

62.2% di *responder*, dato sovrapponibile con il trattamento sistemico con pregabalin

> 80% dei *responder* ottiene il PR nel corso delle prime 2 settimane di trattamento

Dati clinici 4 anni di osservazione confermano l'efficacia prolungata nel lungo periodo

Efficace

Lg IASP

Lg EFSN

Key Messages: Facilità di utilizzo

Non necessita di wash-out farmacologico/ Basso rischio di interazioni farmacologiche

Nessuna titolazione

Facile da applicare e da rimuovere

Facilità di utilizzo

Cochrane Library

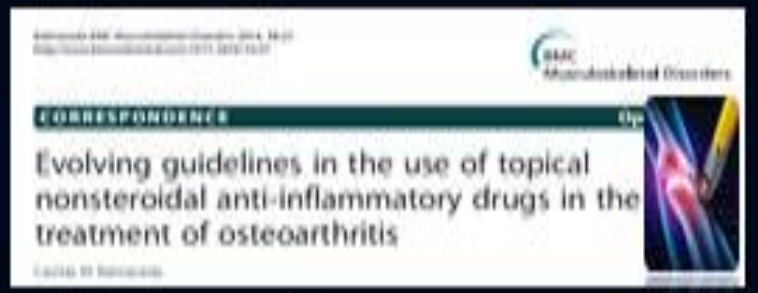
Trusted evidence.
Informed decisions.
Better health.

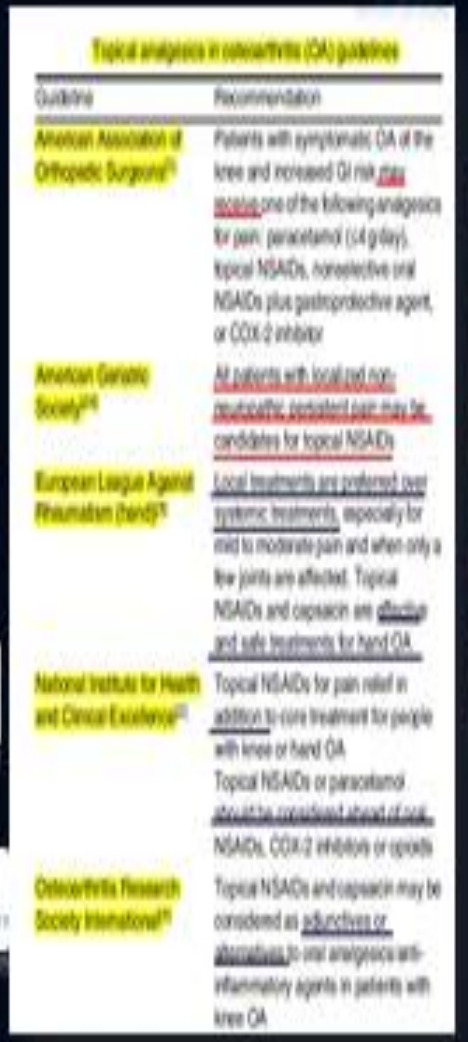
Intervention Review

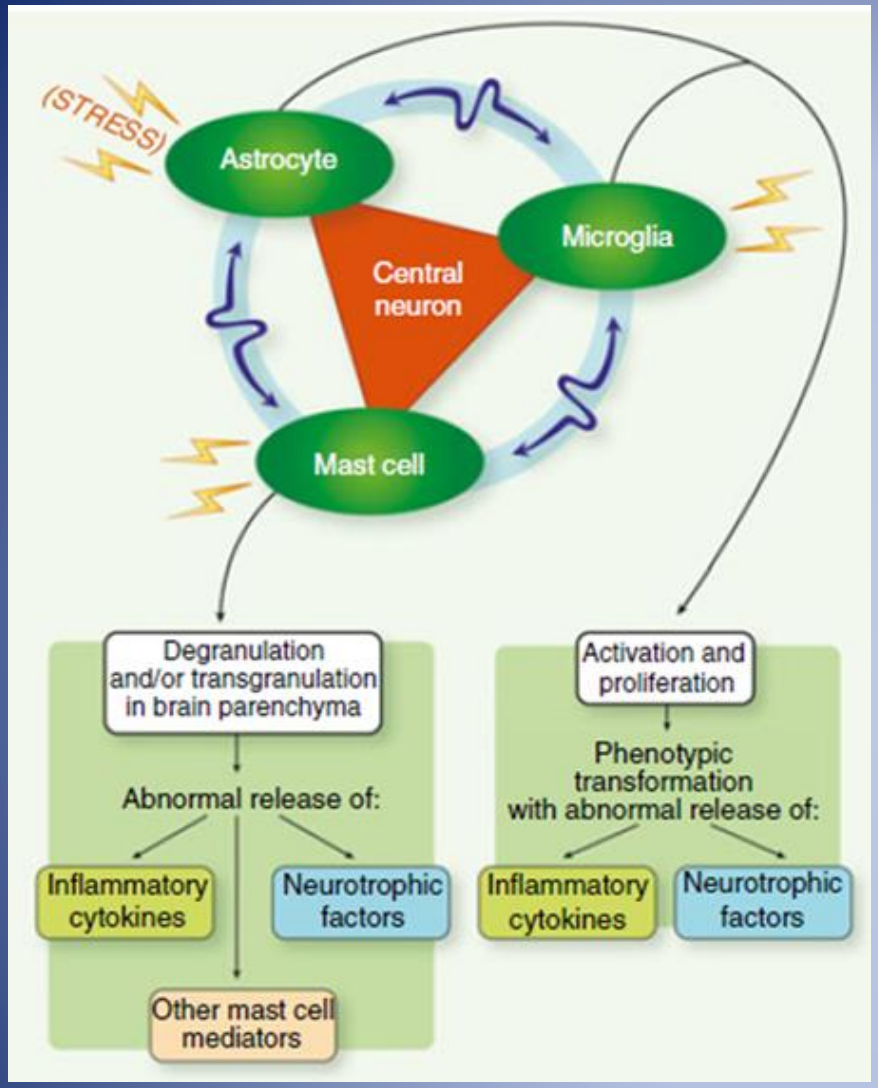
Topical NSAIDs for chronic musculoskeletal pain in adults

Published Online: 12 SEP 2012

- Review di 34 studi.
- Il meccanismo d'azione per cui i FANS topici producono analgesia è **uguale** a quello dei FANS orali ma, poiché **l'attività topica è effettivamente confinata al sito di applicazione**, l'esposizione sistemica, e quindi il **rischio di tossicità GI, CV e renale è risultato molto più basso vs quello orale**
- I FANS topici, particolarmente quelli a base di DF, comparati con quelli orali, hanno prodotto **minori EC** a livello sistemico, **pur mantenendo un'efficacia similare.**



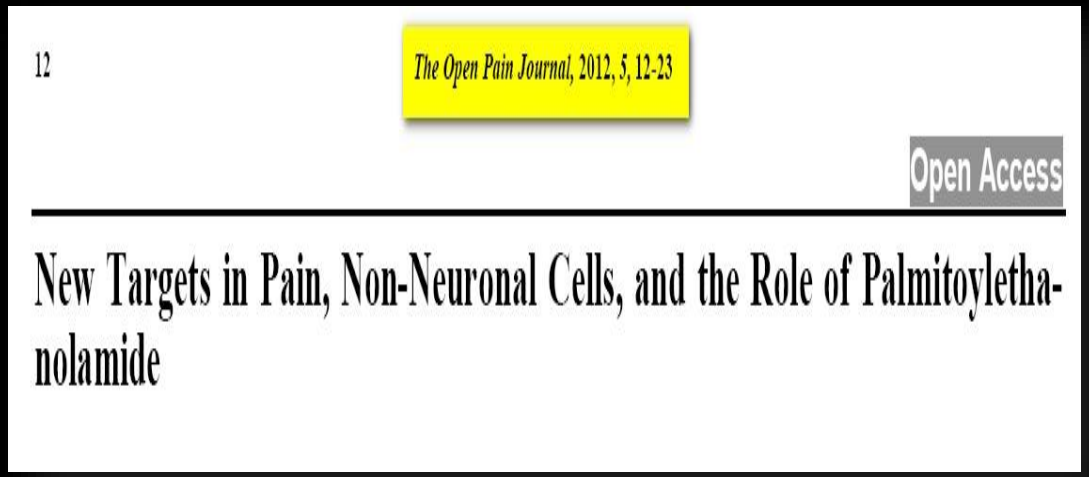




- 610 pz, scarso PR, dolore da differenti etpgns:
- →PEA 600 MG bid/3 W→600 OAD/4 W
- SIGNIFICATIVA" RIDUZIONE NRS (ANCHE IN ASSENZA DI ALTRE TP)
- NO EC

Pain Medicine 2012; *: **–**
Wiley Periodicals, Inc.

Palmitoylethanolamide in the Treatment of Chronic Pain Caused by Different Etiopathogenesis


12

The Open Pain Journal, 2012, 5, 12-23

Open Access

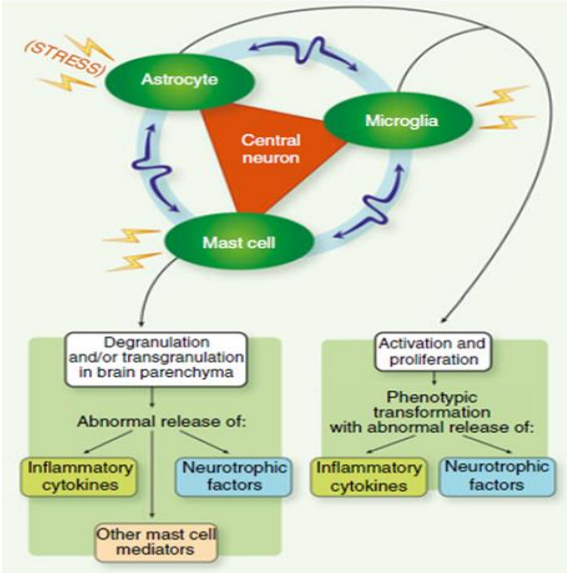
New Targets in Pain, Non-Neuronal Cells, and the Role of Palmitoyletha-nolamide

- SIGNIFICATIVA < INTENSITA' DEL DOLORE
- **RIDUZIONE DEL DOSAGGIO DELLE TP CONVENZIONALI**
- NESSUN EC

NP PERIFERICO	SCIATALGIA 747
LBP 101	NP DIABETICA+ NPH 80
STC 116	TMJD 30
POP 24	***VARI STATI DOLOROSI*** 517
NP CENTRALE	SM 20
POSTSTROKE 20	PELVIC CP
ENDOMETRIOSI, DISMENORREA, C.I. 110	

Pooled Metanalisi 12 studi clinici 1484 pz

Risultati



PEAm e PEAum è efficace nel dolore di varia etiologia (vs controllo: p<0.001)

Pain Physician 2016; 19:11-24 • ISSN 1533-3159

Systematic Review

Palmitoylethanolamide, a Special Food for Medical Purposes, in the Treatment of Chronic Pain: A Pooled Data Meta-analysis

La % di pz che a fine trattamento ha VAS <3 è <u>significativamente maggiore</u> (p<0,0001) <u>nel gruppo PEA (66.8%)</u> vs gruppo controllo (20.9%)

Table 3. *Distribution of patients according to pain etiology.*

	Etiopathogenesis			
	Degenerative	**Neuropathic**	**Mixed**	**Miscellaneous**
Patient number	1174 (79.1%)	170 (11.5%)	82 (5.5%)	58 (3.9%)

Table 1. Patient characteristics.

	Study Design		Gender		Age (years)		Pain Intensity (baseline)		TOTAL
	Open Label	**Double-blind**	**Male**	**Female**	**< 65**	**≥ 65** *	**< 4**	**≥ 4**	
Control	30	266	138	158	251	45	18	278	296 (20%)
m.PEA / u.m.PEA	703	485	460	708	742	446	35	1153	1188 (80%)
TOTAL	733 (49%)	751 (51%)	598 (41%)	866 (59%)	993 (67%)	491 (33%)	53 (4%)	1431 (96%)	1484

Table 2. *Clinical trials selected for pooled meta-analysis.*

Source of pain	Study Design	n°	Regimen of m.PEA or u.m.PEA	Published Studies and Proceedings	Unpublished Studies
Lumbosciatica	Double blind, two doses, randomized, controlled m.PEA vs placebo + NSAIDs when needed	636	1st arm 300mg/day m.PEA x 21 days 2nd arm 600mg/die m.PEA x 21 days +NSAIDs when needed	Guida G et al. 2010 (42)	
Carpal tunnel syndrome in diabetic patients	Open controlled randomized m.PEA vs no treatment	40	1200mg/day m.PEA x 60 days	Assini A et al. 2010 (68)	
Carpal tunnel syndrome-course pre-and post-operative	Open controlled randomized u.m.PEA vs no treatment	50	1200mg /day u.m.PEA x 60 days		Evangelista M. 2015a
Carpal tunnel syndrome	Double blind, randomized, controlled u.m.PEA vs placebo + NSAIDs when needed	48	1200mg/day u.m.PEA x30 days + NSAIDs when needed		Zanette G 2015b
Radiculopathy (331) Osteoarthritis (54) Herpes Zoster (44) Diab. Neuropaty (32) Failed back surgery (76) Oncologic (22) Other diseases (51)	Open-label	610	1200mg/day u.m.PEA x 21 days followed by 600mg/ day u.m.PEA x 30 days (+anticonvulsant, opioid and rescue drugs* except 90 patients)	Gatti A et al. 2012 (69)	

Low back pain	Open-label	20	1200mg/day u.m.PEA + Oxyicodone x 30 days	Desio P. 2011 (70)	
Diabetic neuropathy (11) Postherpetic neuralgia (19)	Open-label	30	1200mg/day u.m.PEA +Pregabalin x 45 days	Desio P. 2010 (71)	
Diabetic neuropathy,(23) Traumatic neuropathy (7)	Open-label	30	1200mg/day u.m.PEA x 40 days	Cocito D et al. 2014 (72)	
Post stroke	Open controlled, randomized, u.m.PEA + Physiotherapy vs only Physiotherapy	20	1200mg /day u.m.PEA x 60 days followed by 600mg/ day u.m.PEA x 30 days	Parabita M et al. 2011 (73)	
Neuropathic pain induced by chemotherapy	Open label	10	1200mg /day u.m.PEA x 60 days		Spada S. 2015c
Multiple Sclerosis	Double blind, randomized, controlled u.m.PEA vs placebo	27	600mg/day u.m.PEA x 365 days	Montella S et al., 2014 (74)	
Charcot Marie Tooth	Open label	12	1200mg/day u.m.PEA x 80 days		Putzu GA. 2015d.

Pain Physician 2015; 18:E863-E876 • ISSN 2150-1149

Narrative Review

mevg@2019

Chronic Pain in the Elderly: The Case for New Therapeutic Strategies

Osteoarthritis	Temporomandibular joint	• greater pain score reduction • better maximum mouth opening • greater tolerability	104
Chronic Pain	Lumbosciatica	• pain score reduction • reduced disability	98
	Lumbosciatica	• pain score reduction • reduced exposure to anti-inflammatory or analgesic drugs	105
	Various etiologies	• pain score reduction	107
	Cervicobrachial or sciatic pain	• reduced chronic pain score • reduced pain impact on emotional state • reduced pain impact on employment	108
	Low back pain	• pain score reduction • reduced disability	100
	Diabetic neuropathy and postherpetic neuralgia	• pain score reduction • reduced disability	101
	Carpal tunnel syndrome	• reduced median nerve latency time • minor Tinel's sign presence • reduced discomfort	102

Pain Physician 2015; 18:E863-E876 • ISSN 2150-1149

Narrative Review

Chronic Pain in the Elderly: The Case for New Therapeutic Strategies

Neuropathic pain	Chemotherapy-induced neuropathy	• pain score reduction • increased amplitude of foot-LEPs, sural-SNAPs, peroneal-CMAPs	106
	Lumbosciatica	• pain score reduction • quality of life improvement	109
	Diabetic polyneuropathy	• pain relief • reduced neuropathic symptoms	110
	Diabetic and traumatic polyneuropathy	• pain relief • reduced neuropathic symptoms • quality of life improvement	111

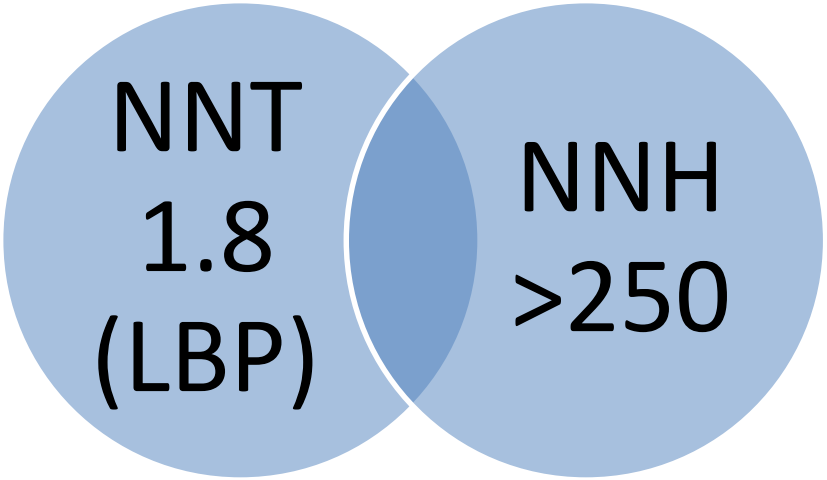
106. Truini A,. Palmitoylethanolamide restores myelinated-fibre function in patients with chemotherapy-induced painful neuropathy. *CNS Neurol Disord Drug Targets* 2011; 10:916-920
109. Domínguez CM N-palmitoylethanolamide in the treatment of neuropathic pain associated with lumbosciatica Pain Manage 2012; 2:119-124.
110. Schifilliti C, Micronized palmitoylethanolamide reduces the symptoms of neuropathic pain in diabetic patients. Pain Res Treat 2014;
111. Cocito D Short-term efficacy of ultramicronized palmitoylethanolamide in peripheral neuropathic pain. Pain Res Treat 2014; 2014:854560.

NNT\NNH 2099 PZ Gianfelice V 2013

Pain Physician 2015; 18:E863-E876 • ISSN 2150-1149

Narrative Review

Chronic Pain in the Elderly: The Case for New Therapeutic Strategies



1. Pain Relief maggiore
2. Ricorso ad analgesici ed antinfiammattori ridotto
3. Riduzione dei segni e sintomi neuropatici
4. Recupero della disabilità, della quotidianità e miglioramento globale della QoL

:

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Narrative Review

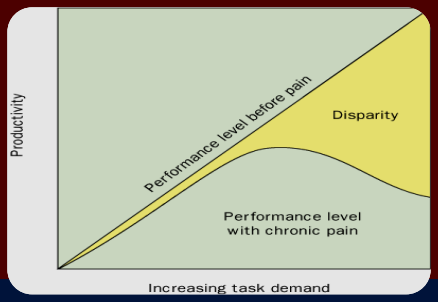
Chronic Pain in the Elderly: The Case for New Therapeutic Strategies

Among therapies aiming at preserving the functionality of non-neuronal cells, PEA, with its **high efficacy/risk ratio**, may be an **excellent co-treatment** for the **ever-growing elderly population with chronic pain**.

METODOLOGIA DI STRUTTURAZIONE E GESTIONE DI UN PROTOCOLLO TERAPEUTICO

OBBIETTIVI

- Realistici
- Orientati sui desiderata del pz
- Recupero della disabilità
- RECUPERO DELLA QUOTIDIANITA'



TITOLAZIONE

- Molecole interferenti con il meccanismo
- Bassi dosaggi, formulazioni IR, se disponibili, ad orario e RD
- Schemi semplici per il pz o per il familiare, rispettosi dello schema di giornata

MONITORAGGIO

- **PGIC, EC, RD, RSV**
- **COSA VORRESTI MIGLIORARE?**
- **T1 A 7 GG MAX**
- **T2 TRA 15 E 30GG**
- **A TERAPIA STABILIZZATA CONTROLLI CON CADENZA BI-TRIMESTRALE**

TAPERING

- **INIZIARE SE, SECONDO IL PZ, SONO CENTRATI, IN MANIERA STABILE GLI OBBIETTIVI**
- **PROCEDERE RIDUCENDO GRADUALMENTE IL DOSAGGIO TOTALE GIORNALIERO MA RISPETTANDO LA COPERTURA DELLE 24 ORE**
- **STABILIRE, AL PARI DELLA TITOLAZIONE, UNO SCHEMA DI MONITORAGGIO "SERRATO"**

Q.o.L

QUOTIDIANITA’

APPROPRIATEZZA:
a)MECHANISM ORIENTED
b)FENOTIPO DEL DOLORE

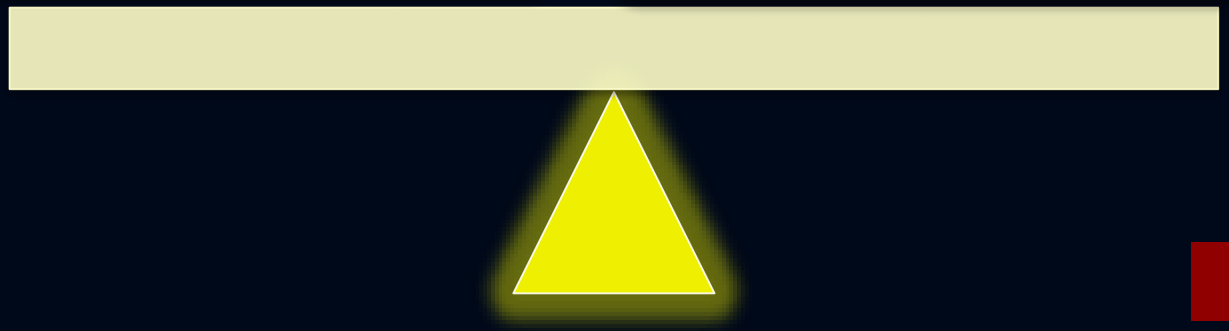
PRATICABILITA’:
TANTO MIGLIORE QUANTO PIU’ SEMPLICE

TOLLERABILITA’:
a)TITOLAZIONE b)MONITORAGGIO
c)TAPERING d)MULTIMODALITA’

ADEGUATEZZA:
TANTO MAGGIORE QUANTO PIU’ ORIENTATA SUGLI OBBIETTIVI DEL PAZIENTE

EFFICACIA ANALGESICA:
TANTO MAGGIORE QUANTO PIU’ MIRATA SUL/SUI BERSAGLIO/I PATOGENETICO/I

ADERENZA ALLA TERAPIA



Conclusioni 2

- A nostra conoscenza questo è il **primo contributo congiunto** tra MMG e Terapisti del Dolore
- La limitata casistica, unitamente ai favorevoli risultati raggiunti, sono **stimolo per poter ampliare questa sinergia «pilota» nello specifico setting del MMG**
- Ciò potrà avvenire solo **continuando a condividere sempre più le nostre realtà**, rendendo possibile una **attuazione concreta di quanto postulato dalla Legge 38/2010**

sabato 8

Sala DALÌ - MIRÒ

08.30 - 10.00

EMICRANIA E ALGIE CRANIO-FACCIALI:
LE NUOVE TERAPIE
Sessione congiunta: SISC, AISD, WFNS, FIMMG
Moderatori: *Francesco Pierelli, Maurizio Evangelista, Maurizio Pirro*

10.30 - 12.00

NEUROINFIAMMAZIONE E DOLORE
Sessione congiunta: AISD, FIMMG
Moderatori: *Stefano Coaccioli, Maurizio Evangelista*

12.00 - 13.30

DOLORE NEUROPATICO E REAL LIFE SETTING
i tre passaggi chiave per una gestione utile ed efficace
Sessione congiunta: AISD, FIMMG
Moderatori: *Walter Marrocco, Maurizio Evangelista*

Voglio concludere ripartendo da dove ho iniziato: auspicando, cioè che questa sinergia, ai suoi albori, prosegua e si consolidi sempre più.

Ed è per questo che ho il piacere di invitarvi tutti al prossimo focus day, che ha visto nascere formalmente la nostra interazione.

Vi aspetto a Roma, il …parleremo di…

SAVE THE DATE

EVENTO ACCREDITATO ECM

FOCUS DAY # 11

LE QUESTIONI APERTE:
QUALI SPECIALISTI, QUALI TERAPIE, QUALE TIMING

DOLORE, OSTEOPOROSI E QUALITA' DELLA VITA: LA NECESSITA' DI UNA SINERGIA INTER E MULTIDISCIPLINARE PER UN PARADIGMA DI SANITA' PUBBLICA

Direttore Scientifico:

Prof. Maurizio Evangelista

Roma, 18 gennaio 2020

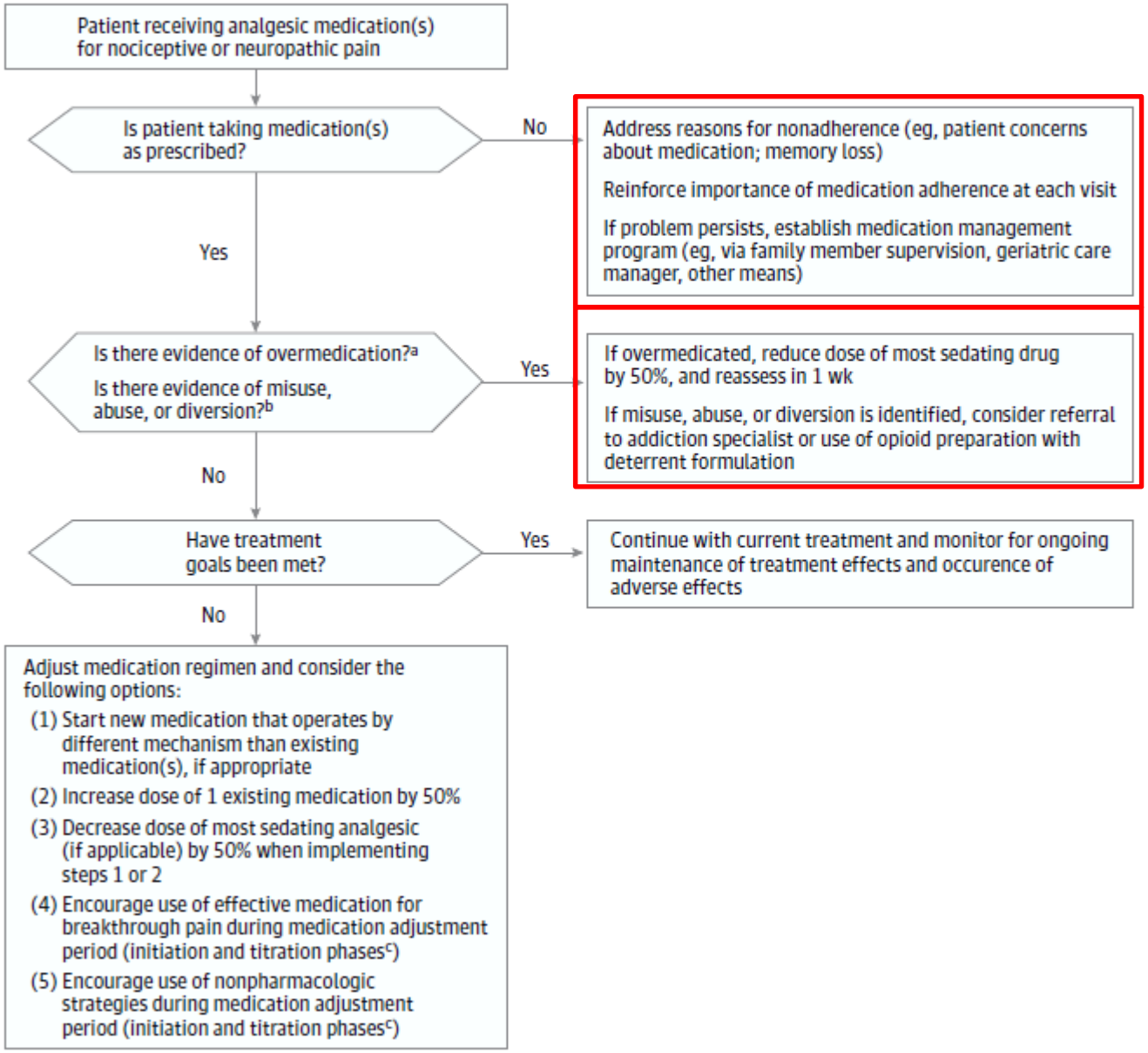
Sede:

Luiss

Viale Romania, 32 - Roma

Segreteria Organizzativa: ZEROSEICONGRESSI SRL - Via Benaco 15 - 00199 Roma - tel. +39068416681 - E-mail: info@zeroseicongressi.it

Figure 2. Approach for Monitoring Pain Management and Adjusting Medication for Older Adults Already Taking Analgesic Medications



[a] Obtain both patient and proxy data whenever possible: assess for history and physical examination evidence of gait disturbance, falls or near falls, mental status changes (confusion, lethargy, mental slowing, attention problems); change in gastrointestinal or genitourinary function: assess for other adverse effects based on knowledge of adverse-effect profile of prescribed medication(s).

[b] Recommend routine screening for misuse/abuse behaviors, periodic urine testing; consider treatment agreements. Review data from prescription drug monitoring programs regularly in states that have them.

[c] Initiation indicates selection of starting dose and frequency of administration; titration indicates adjustment of medication dose to achieve optimal level of analgesia (see Table 1).