

Chronic Pain and Psychiatric Comorbidities in Fibromyalgia and Temporomandibular Disorders: A Systematic Review

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Affiliations and Disclosures

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- Previously employed by, PinneyAssociates (2014-2018), a consulting firm that provides scientific and regulatory advice to pharmaceutical industry (risk management, abuse liability OTC switch) and tobacco companies (vapor products only/harm reduction).

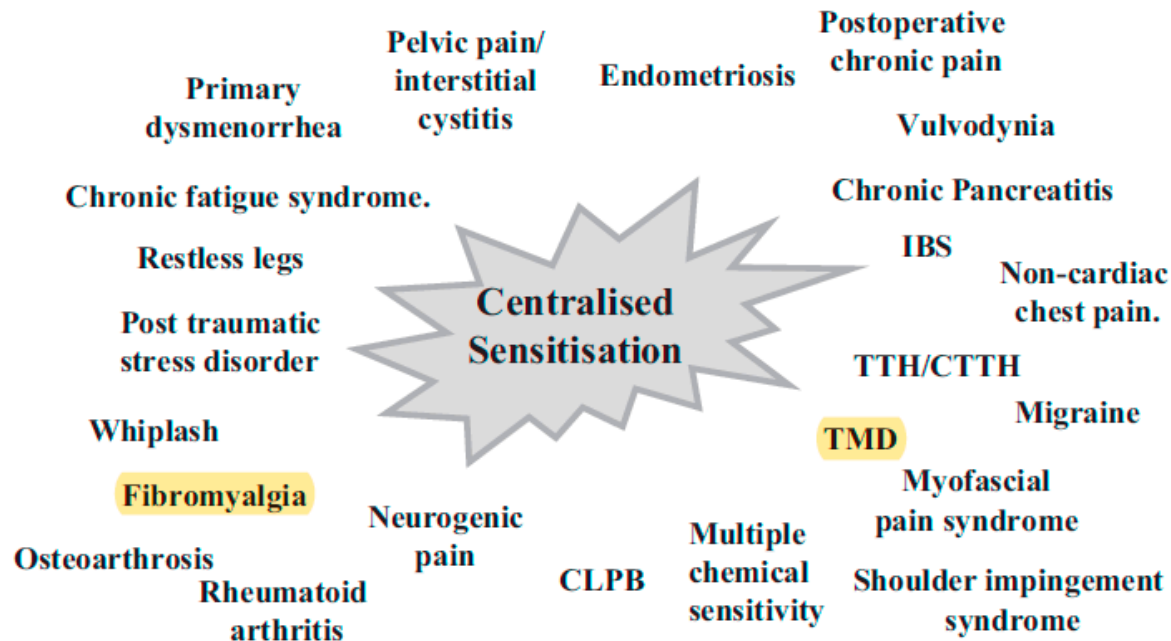
Background – Index Disorders

- Fibromyalgia (FM)
 - Musculoskeletal pain disorder often including widespread muscle pain and tenderness
 - **Diagnosis:** American College of Rheumatology (ACR; Wolfe et al., 2011; Arnold et al., 2019)
 - **Prevalence:** 0.2 to >11% (estimates can vary considerably; Marques et al., 2017)
 - Gender differences (Wolfe et al., 2018)
- Temporomandibular Disorders (TMD)
 - Orofacial pain disorder involving the temporomandibular joint
 - **Diagnosis:** Research Diagnostic Criteria (RD; Schiffman et al., 2014)
 - **Prevalence:** 5 to 12% (NIH, 2019)

Background – Index Disorders and Central Sensitization

Assessment and manifestations of central sensitisation

L. Arendt-Nielsen et al.



Background – Comorbid Disorders

- FM and TMD are overlapping conditions that share many key symptoms (generalized pain, bowel complaints, headache; Aaron et al., 2000; Plesh et al., 1996)
- Why examine comorbidities?
 - Better understand the patient experience:
 - patient symptoms and pain perception
 - disability and reduce quality of life
 - Inform diagnosis of index disorder (e.g., FM or TMD)
 - Examine shared etiological pathways across conditions
 - Refine treatment approach

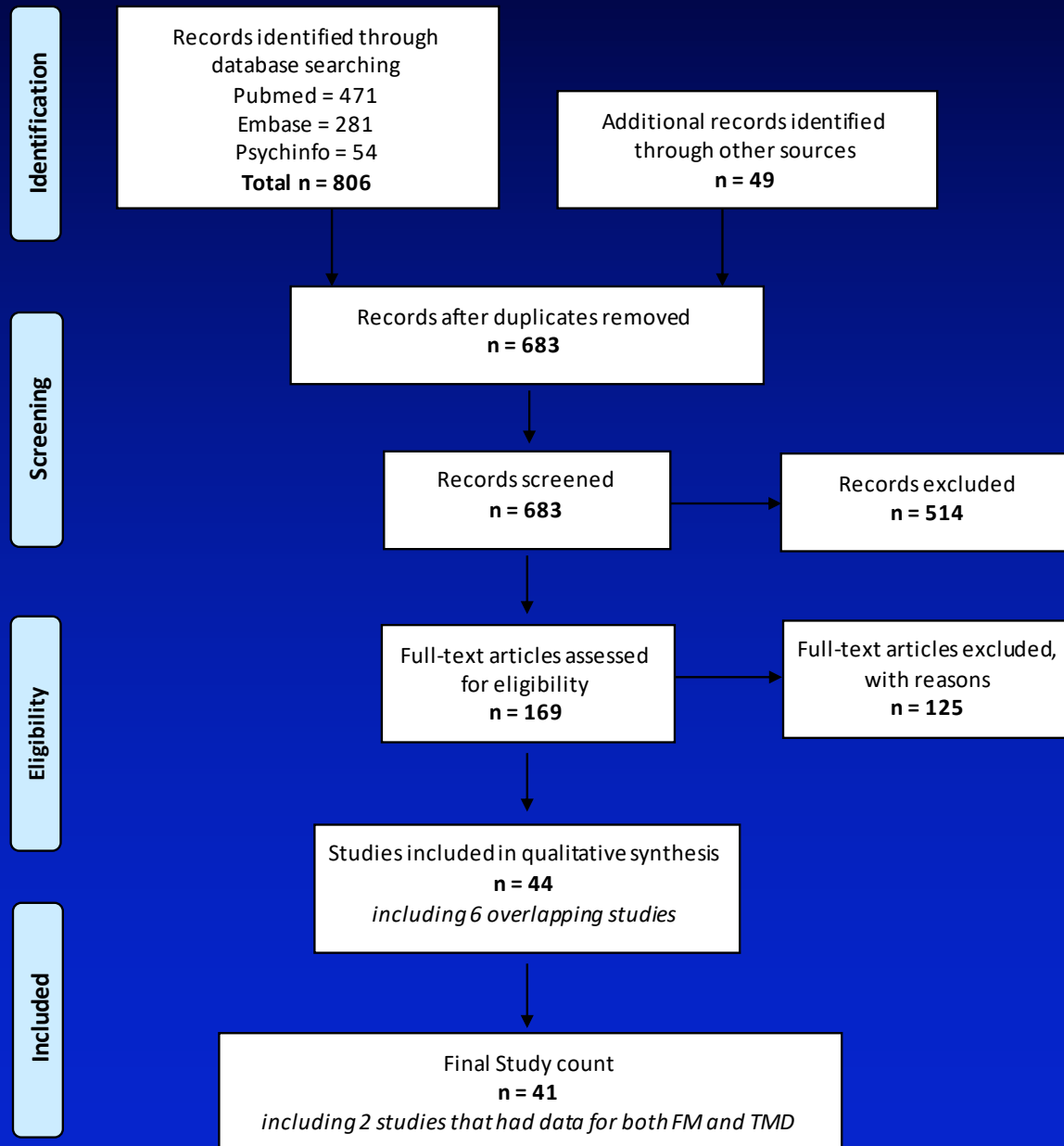
Objectives

- Provide overview of published literature examining chronic pain and psychiatric comorbidities in FM and TMD
- Determine the incidence and/or prevalence of these comorbidities in FM and TMD

Methods

- **Systematic Review Search Strategy**
 - PROSPERO registration #CRD42019133249
 - PubMed, PsychInfo, and Embase databases search through April 27, 2019.
 - **Search terms:** (fibromyalgia or temporomandibular disorders) AND (comorbidity or comorbid) AND (incidence or prevalence or cross-sectional or cohort) AND (psychiatric or mental health disorder or chronic pain)
- **Inclusion criteria**
 - Criteria-based diagnosis of FM (ACR) and TMD (DC)
 - Psychiatric outcomes – Mood, Anxiety, Personality disorders diagnosed via structured interview using a standardized assessment tool (Løge-Hagen et al., 2019)

PRISMA Flow Diagram



Excluded Studies (N = 125)

- **Diagnostic criteria did not meet standards (75% of studies excluded: 95 studies)**
 - **Self-report of psychiatric disorders (47 studies)**
 - **FM not diagnosed with ACR criteria (33 studies)**
 - **TMD not diagnosed with RDC criteria (15 studies)**
- **Prevalence/incidence of chronic Pain/Psychiatric disorders not assessed (15 studies)**
- **Not a research study/not English/FM or TMD not assessed (14 studies)**
- **TMD diagnosis acute only (1 study; Lorduy et al., 2013)**

Overview of Studies (N = 41)

- **Study design:** cross-sectional
 - Some studies were cohort studies that compared the index disorder group to a control, non-FM/TMD group
 - Only cross-sectional data were included from FM/TMD group
- **Publication years**
 - 1992 to 2018
- **Study locations**
 - US (14)
 - Italy (10)
 - Brazil (4)
 - Turkey (4)
 - Other countries: Canada, Germany, Israel, Norway, Saudi Arabia, Spain, and Sweden

Overview of Study Participants

- Participants were recruited from outpatient clinic settings (convenience sampling – a subset were consecutive sampling)
- **Sample size**
 - 22 to 77,087 (median = 100)
- **Mean participant age**
 - Adults 33 to 58 years (median = 47.2)
- **Gender**
 - 40/41 studies women were majority
 - Nearly half of studies included only women (n=18)
- **Disease duration**
 - 3.9 to 11.43 years (median = 7.72)

Overview of Results

| | | Comorbid Disorder | |
|----------------|---------------------|------------------------------|-----------------------------|
| | | Chronic Pain (22 studies) | Psychiatric (25 studies) |
| Index Disorder | FM (37 studies) | 13 studies | 24 studies |
| | TMD (10 studies) | 9 studies | 1 study |

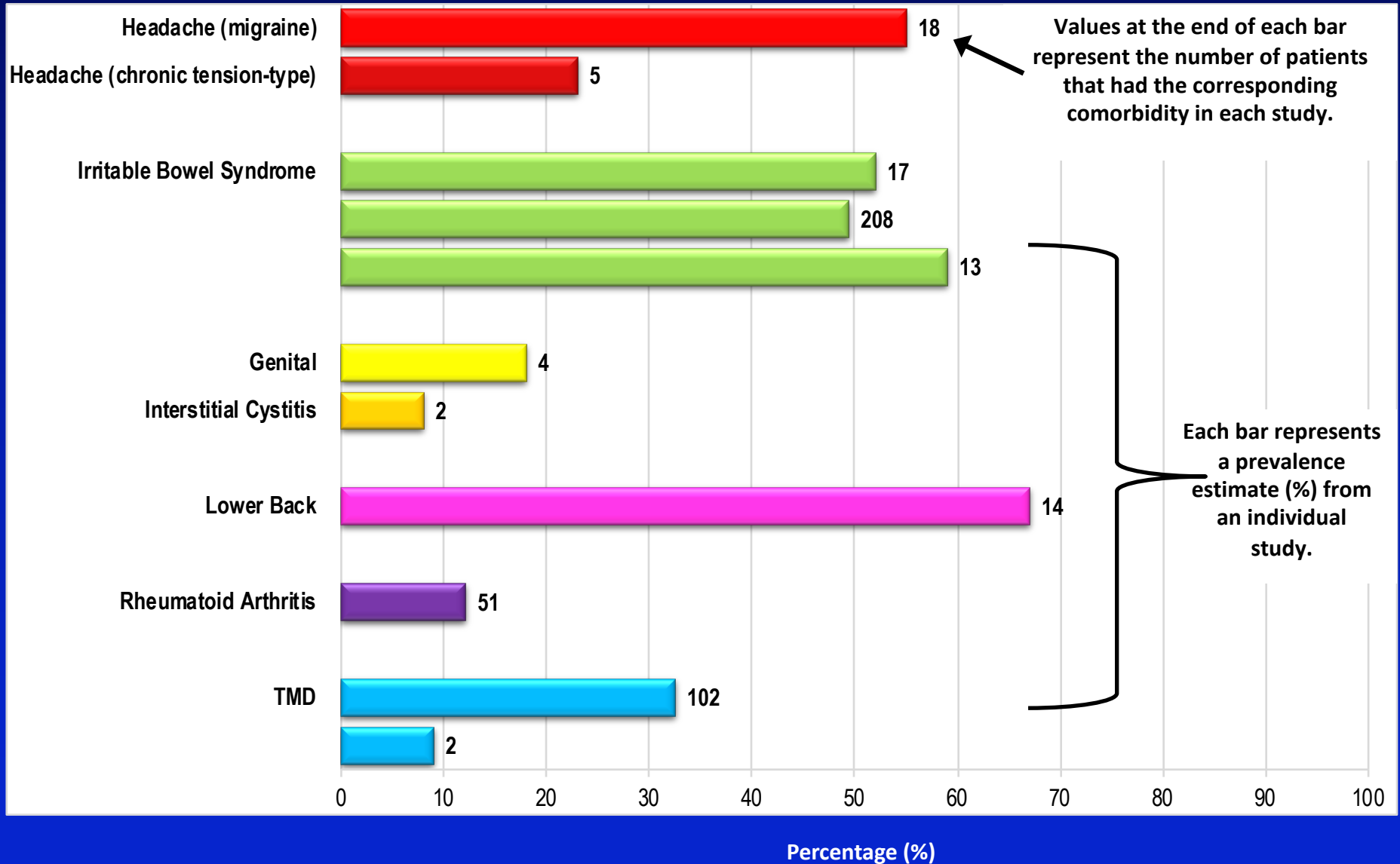
Study counts across cells do not total 41 due to overlapping study data sets (6 studies) and the inclusion of both FM and TMD patients in 2 studies (Aaron et al., 2000; Plesh et al., 1996).

FM and Chronic Pain Comorbidities

| | | Comorbid Disorder | |
|----------------|-----|-------------------|-------------------|
| | | Chronic Pain | Psychiatric |
| Index Disorder | FM | 13 studies | 24 studies |
| | TMD | 9 studies | 1 study |

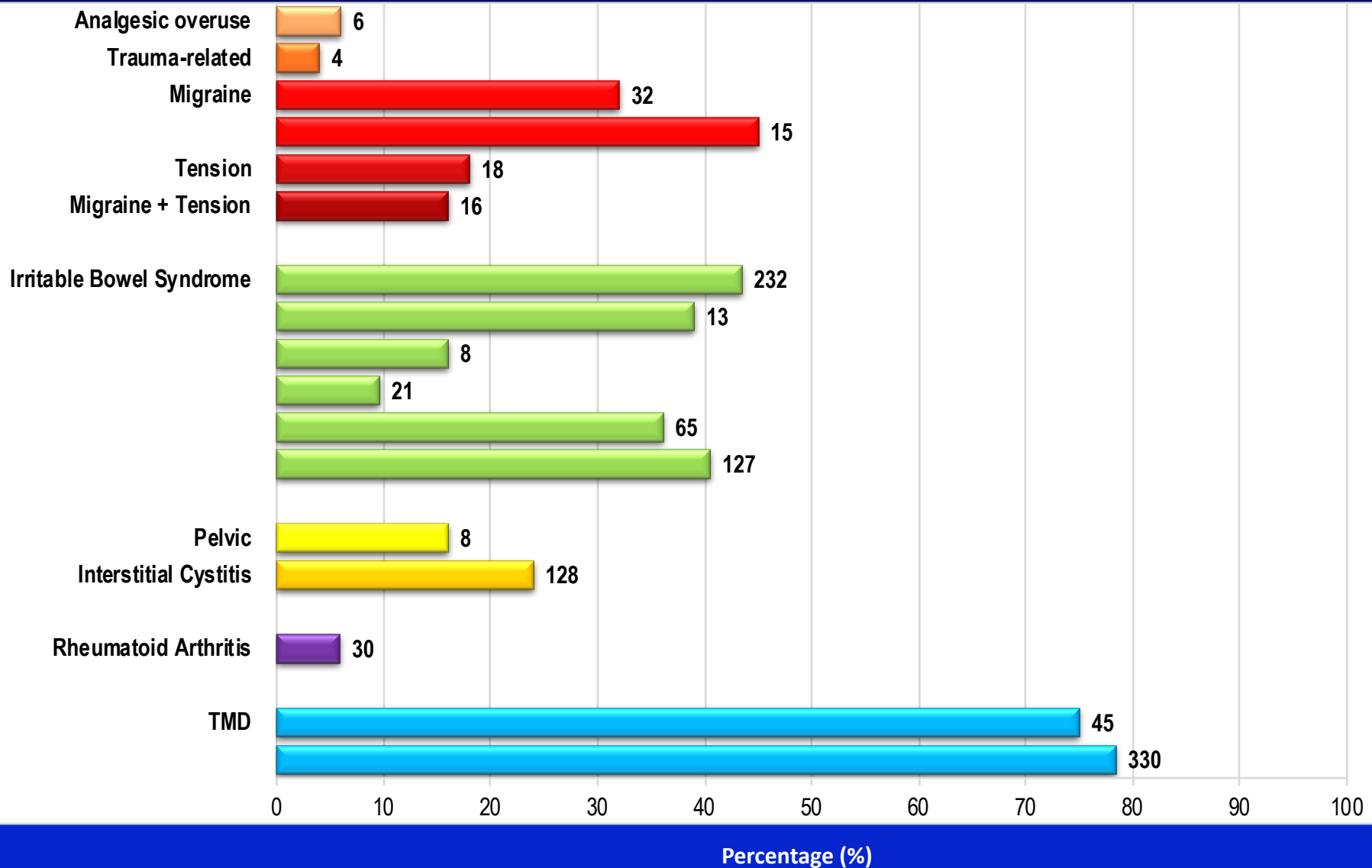
FM and Chronic Pain

Lifetime Prevalence (4 studies)



FM and Chronic Pain

Current Prevalence (10 studies)

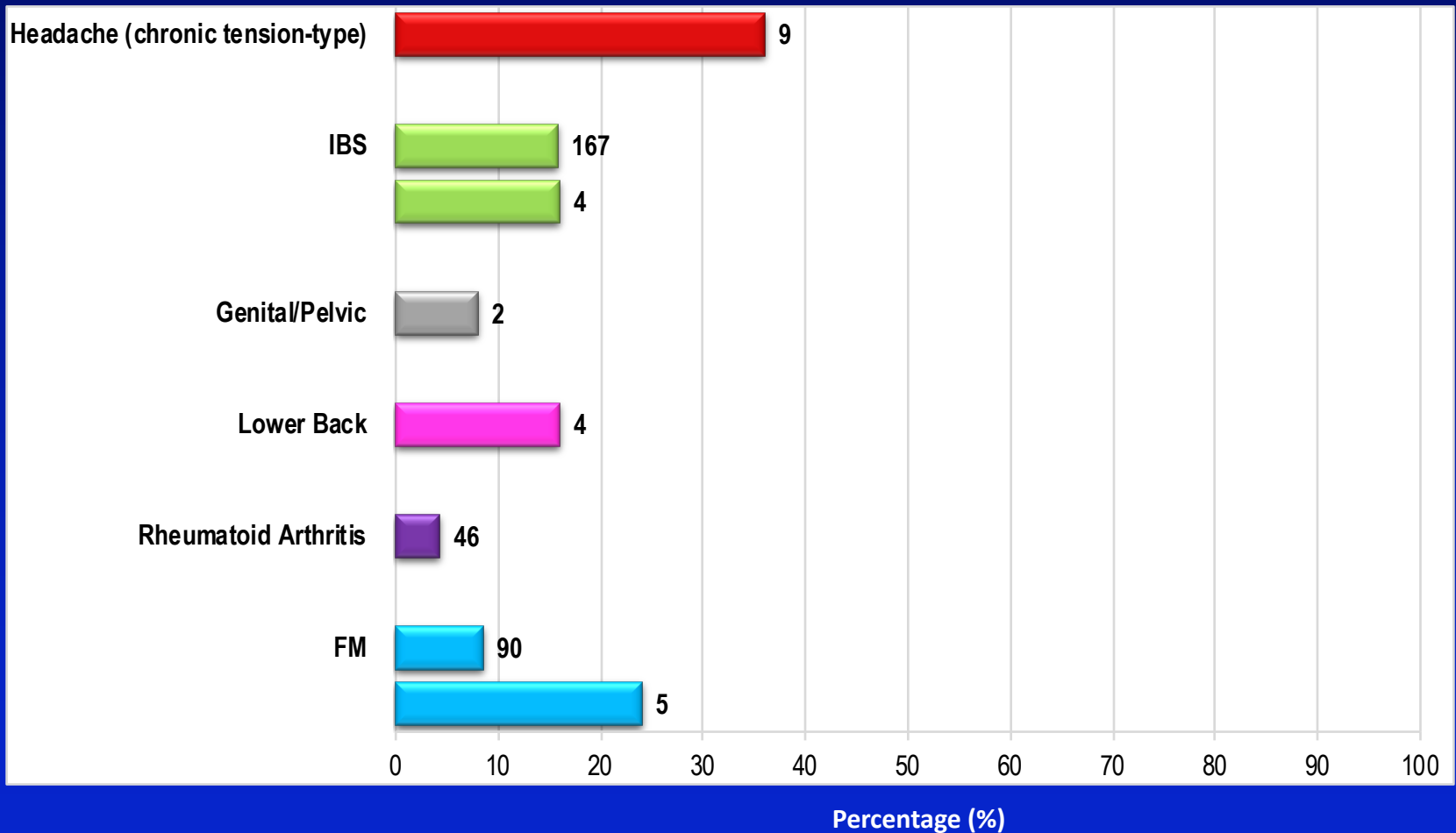


TMD and Chronic Pain Comorbidities

| | | Comorbid Disorder | |
|----------------|-----|-------------------|-------------|
| | | Chronic Pain | Psychiatric |
| Index Disorder | FM | 13 studies | 24 studies |
| | TMD | 9 studies | 1 study |

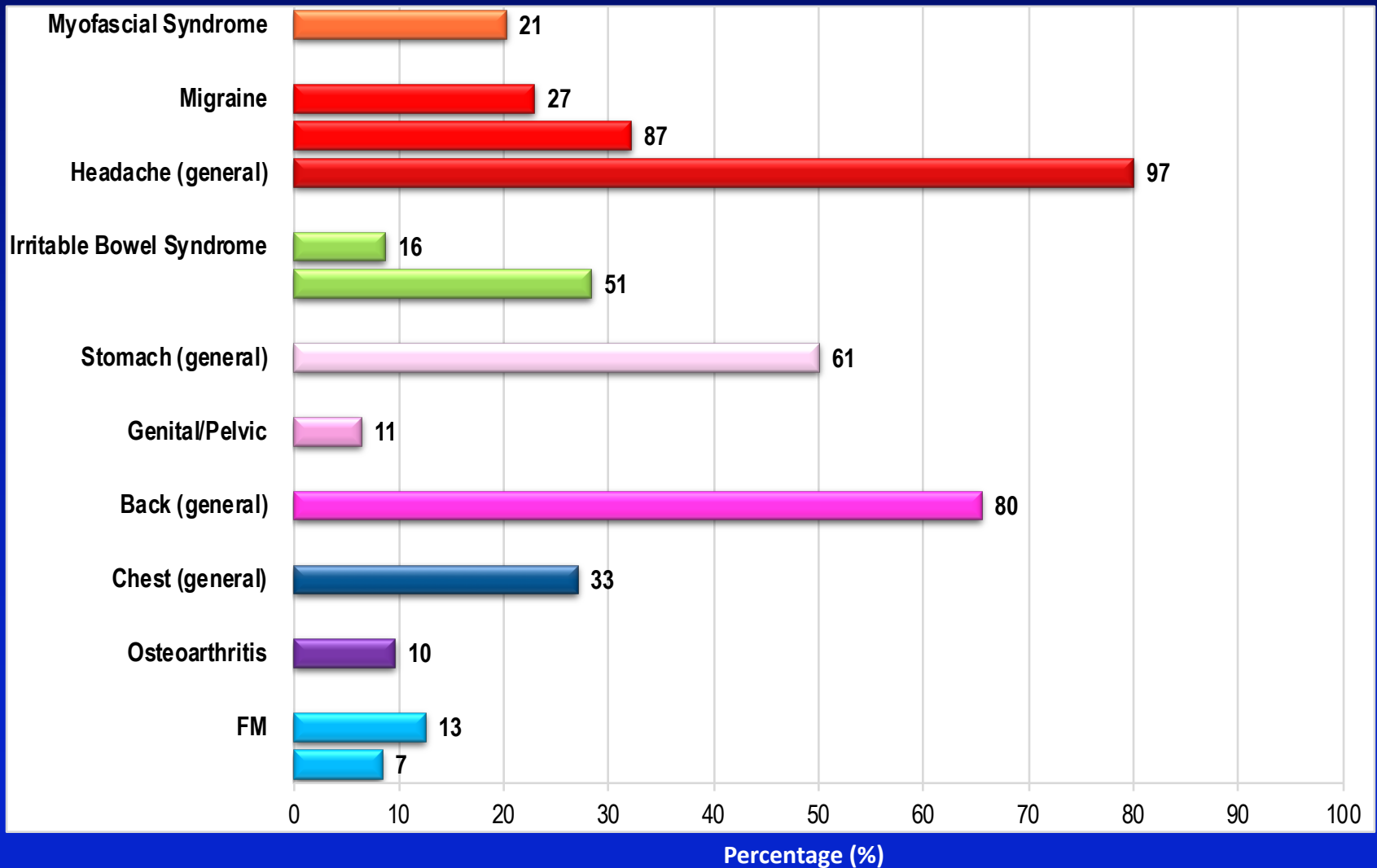
TMD and Chronic Pain

Lifetime Prevalence (2 studies)



TMD and Chronic Pain

Current Prevalence (7 studies)

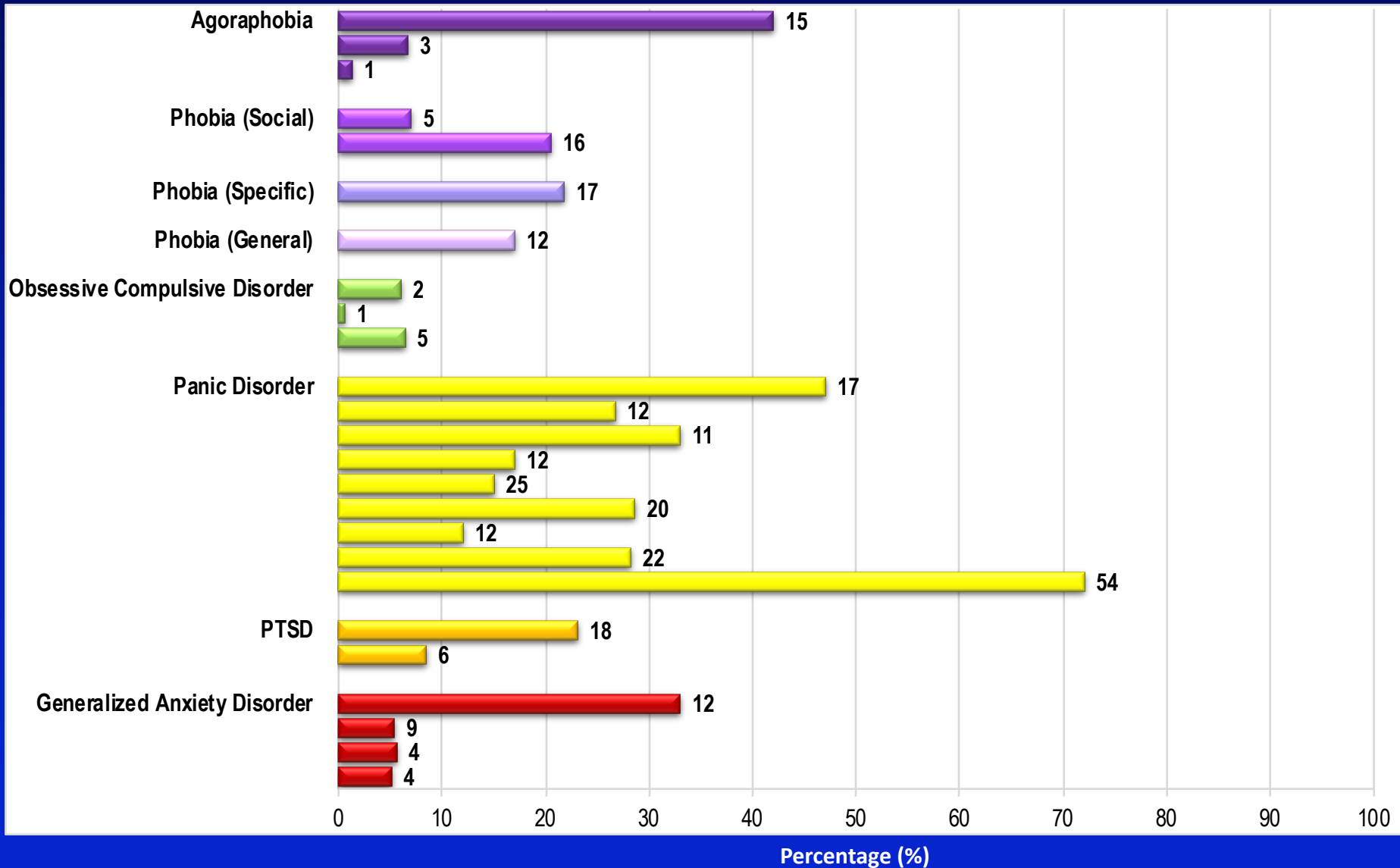


FM and Psychiatric Comorbidities

| | | Comorbid Disorder | |
|----------------|-----|-------------------|-------------|
| | | Chronic Pain | Psychiatric |
| Index Disorder | FM | 13 studies | 24 studies |
| | TMD | 9 studies | 1 study |

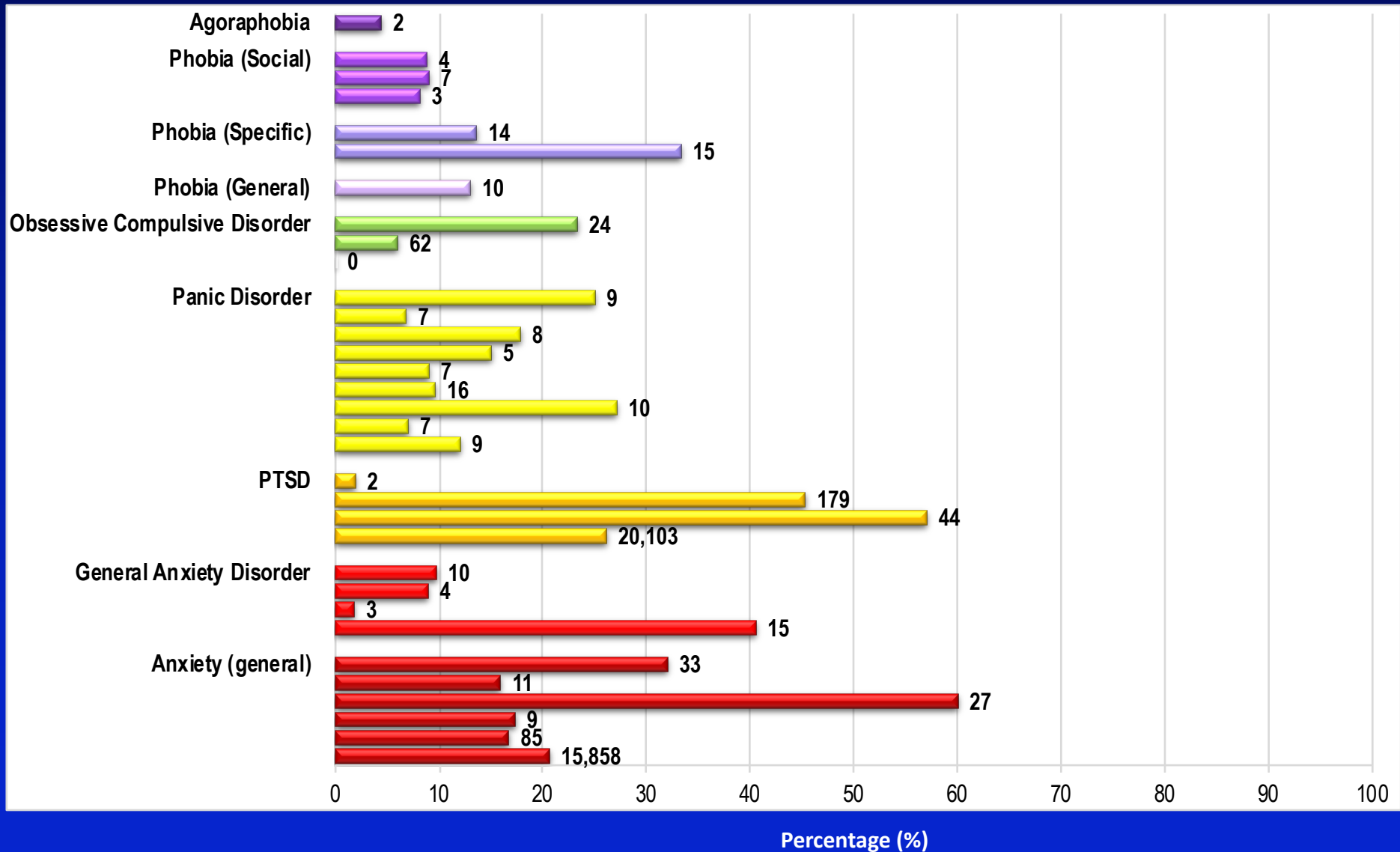
FM and Anxiety Disorders

Lifetime Prevalence (10 studies)



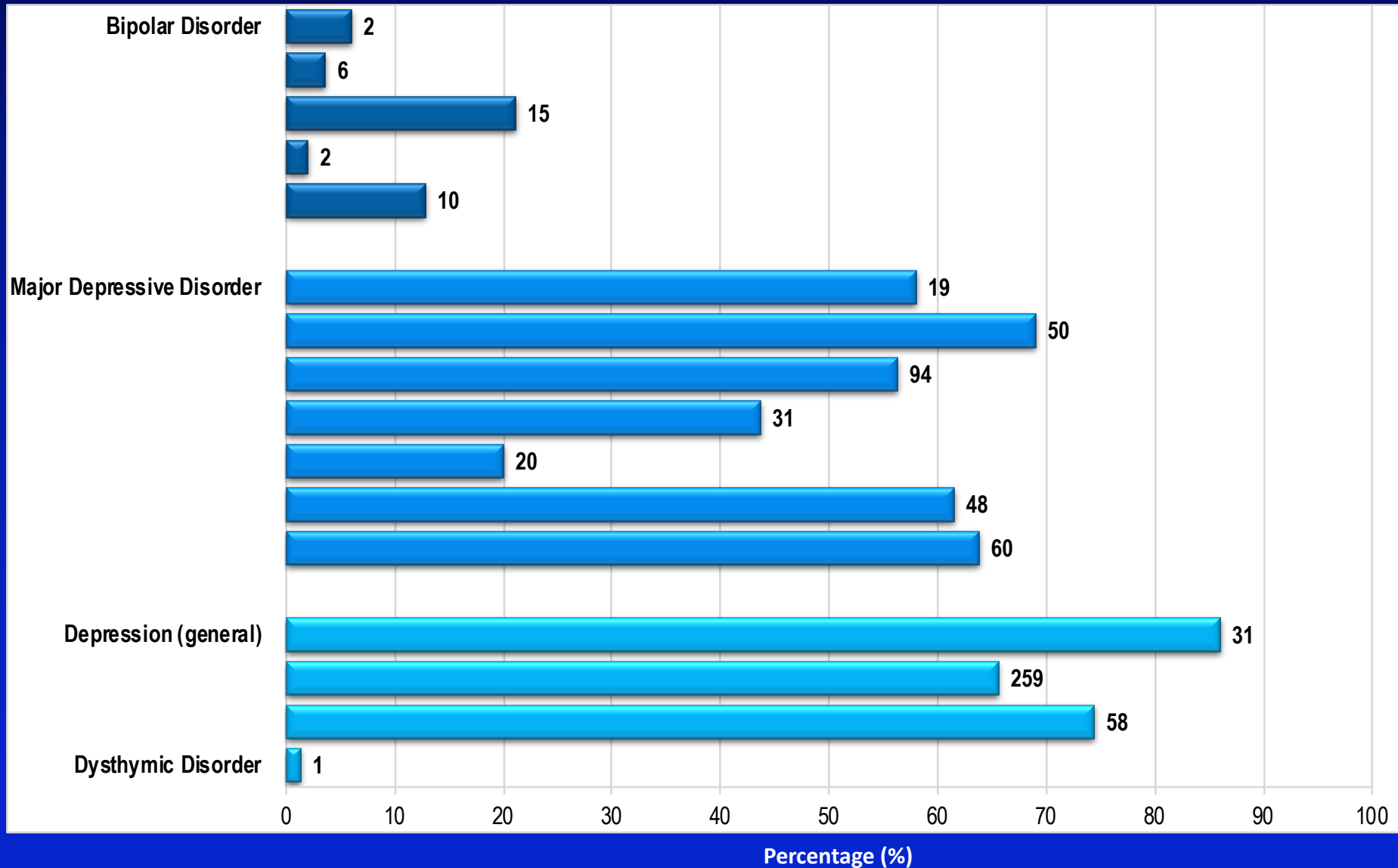
FM and Anxiety Disorders

Current Prevalence (16 studies)



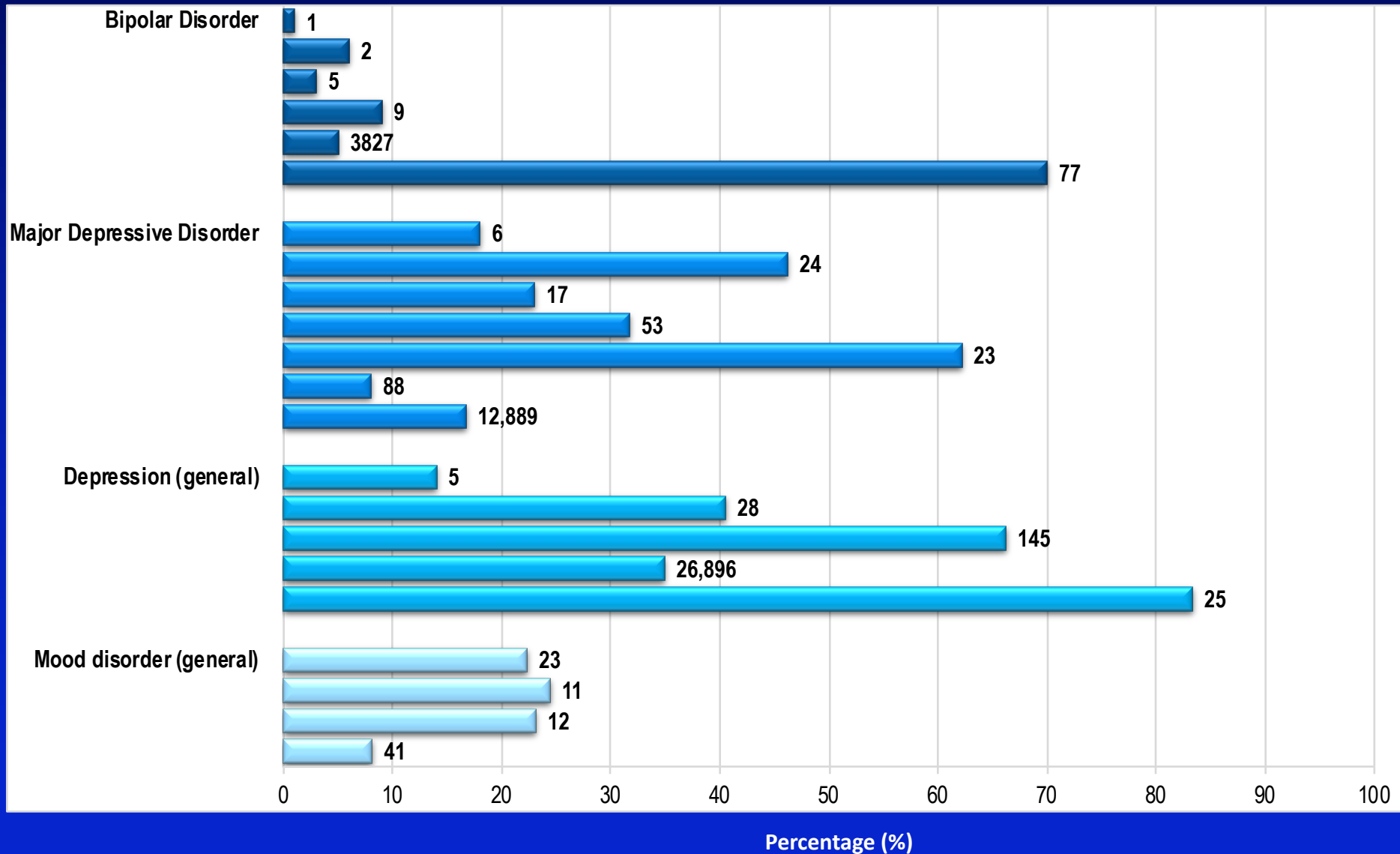
FM and Mood Disorders

Lifetime Prevalence (15 studies)



FM and Mood Disorders

Current Prevalence (15 studies)



TMD and Psychiatric Comorbidities

| | | Comorbid Disorder | |
|----------------|-----|-------------------|-------------|
| | | Chronic Pain | Psychiatric |
| Index Disorder | FM | 13 studies | 24 studies |
| | TMD | 9 studies | 1 study |

TMD and Psychiatric Disorders- Prevalence 1 study

- Nifosi et al., 2007 (N=63) assessed **current** psychiatric comorbidities:
 - **GAD** – 9.5% (n=6)
 - **MDD** – 17.5% (n=11)
 - **Panic Disorder** – 6.3% (n=4)

Summary of Findings

- All 41 studies cross-sectional and included adult patients from outpatient clinics
- Most included women in middle-age and focused on FM (n=37) rather than TMD (n= 10)

Listed comorbidities included prevalence estimates >30% in at least 2 reviewed studies

| | Chronic Pain | Psychiatric |
|-----|-----------------------|-----------------------------|
| FM | IBS TMD | Depression PTSD |
| TMD | Headache Disorders | Not applicable (1 study) |

Limitations

- Small (41) number studies on prevalence (none on incidence).
- Potential for selection bias (sample size 100 or less for most studies, patients recruited through convenience sampling)
 - Methodological trade-off: large sample, population-based studies with less specific diagnostic criteria not included
- All or majority of studies focused on women and FM
 - Women tend to report more health symptoms
 - Number of men diagnosed with FM might be higher than previously thought (Wolfe et al., 2018)
- Shifting prevalence rates over time due to evolving diagnostic criteria over last ~30 years (see Arnold et al., 2019)?

Additional Considerations

- Juvenile FM (Yunus and Masi criteria; Ting et al., 2016)
- Temporal order of co-occurring index and comorbid conditions
- Known relationships between comorbidities (e.g., anxiety and depression; Valtri et al., 2012)
- Sleep-related comorbidities
 - Sleep issues a key symptom of FM (Arnold et al., 2019)
 - Two systematic reviews have examined sleep quality and FM or TMD (Keskindag & Karaaziz, 2017; Veiga et al., 2013)

Special thanks to to my invaluable co-reviewers!

Dr. McKenzie Ferguson
(Southern Illinois University Edwardsville
School of Pharmacy)

Dr. Ewan McNicol
(Pharmacy Practice, MCPHS University)

Overview of Included Studies (N=41)

| | First author | Year | Sample size | Dates of data collection | | First author | Year | Sample size | Dates of data collection |
|----|--------------|------------|-------------|--------------------------|----|-------------------------|------|-------------|--------------------------|
| 1 | Aaron | 2000 (FM) | 22 | Jan 1993-Sept 1994 | 21 | Epstein | 1999 | 73 | 1994-1995 (months NR) |
| | Aaron | 2000 (TMD) | 25 | Jan 1993-Sept 1994 | 22 | Genc | 2011 | 50 | NR |
| 2 | Aguglia | 2011 | 30 | June - Dec 2007 | 23 | Goncalves | 2011 | 271 | NR |
| 3 | Al-Harthy | 2017 | 122 | NR | 24 | Gündüz | 2018 | 52 | Feb 2014-May 2014 |
| 4 | Alciati | 2017 | 94 | May 2010-2011 | 25 | Hauser | 2013 | 395 | Feb 2012-July 2012 |
| 5 | Alciati | 2016 | 75 | May 2010-2011 | 26 | Hudson | 1992 | 33 | N/R |
| 6 | Alciati | 2012 | 110 | May 2010-2011 | 27 | Jordani | 2017 | 159 | May 2013-Dec 2013 |
| 7 | Arnold | 2006 | 78 | Sept 1999 -April 2002 | 28 | Kurland | 2006 | 105 | 2002-2003(9 mos) |
| 8 | AROUT | 2018 | 77087 | Oct 2011-Sept 2011 | 29 | Malt | 2000 | 45 | NR |
| 9 | Bazzichi | 2010 | 314 | NR | 30 | Marcus | 2005 | 100 | NR |
| 10 | Bazzichi | 2013 | 100 | NR | 31 | Melo Santos | 2011 | 69 | June 2006-Sept 2008 |
| 11 | Bernatsky | 2005 | 180 | NR | 32 | Nifosi | 2007 | 63 | NR |
| 12 | Bilge | 2018 | 509 | Jan 2012-Aug 2016 | 33 | Ohrbach | 2011 | 185 | May 2006-Nov 2008 |
| 13 | Brooks | 2015 | 219 | 2009-2010 (months NR) | 34 | Plesh (FM) | 1996 | 60 | NR |
| 14 | Burris | 2010 | 1060 | Oct 1997-Nov 2007 | | Plesh (TMD) | 1996 | 39 | NR |
| 15 | Calandre | 2011 | 421 | NR | 35 | Ribeiro | 2004 | 146 | Aug 2001-Dec 2001 |
| 16 | Carta | 2006 | 37 | NR | | Rodriguez- Rodriguez | 2015 | 536 | NR |
| 17 | Carta | 2018 | 71 | March 2015-July 2015 | 37 | Ross | 2010 | 76 | NR |
| 18 | Ablin | 2008 | 77 | NR | 38 | Thieme | 2004 | 115 | NR |
| 19 | Consoli | 2012 | 167 | NR | 39 | Uguz | 2010 | 103 | NR |
| 20 | Dahan | 2016 | 180 | NR | 40 | Walker | 1997 | 36 | Jan 1994-May 1994 |
| | | | | | 41 | Wright | 1997 | 104 | May 1995-May 1996 |