Treating the Whole Patient in Inflammatory Arthritis: An Opportunity for Collaboration

Michael Starr, MD, FRCP©

Division of Rheumatology

Mcgill University Health Center

Mcgill Family Medicine Review Course
December 7, 2022

Disclosures

- Advisory Boards, Honorariums, Clinical Research:

Fresenius Kabi

Janssen

Abbvie

UCB

Novartis

Lilly

Merck

Pfizer

Objectives

- To better understand the role of treating the whole patient in inflammatory arthritis (IA), beyond traditional pharmacotherapy, to improve outcomes
- To raise awareness and improve skills in considering multimorbities in the comprehensive treatment plan of IA patients
- To partner with primary care MD’ s to improve care of these patients

Case

- 59 y.o. male, 3 kids, seropositive RA 4 years
- Overweight, DM2, HTN
- Trying to stop smoking (now 5-8 cigs/day)
- Off work due to RA, financial stress, moody
- Now on HCQ/MTX, but still active disease
- Also takes ASA, HTN meds, oral agents DM, statin
- BP 155/92, CRP 22, LDL 3.45, HDL 1.2, A1-C 7.0

Preparing for a biologic agent……..

What is the ideal management approach (or rather a “wish list”) ?

RA and Multimorbidity- definitions

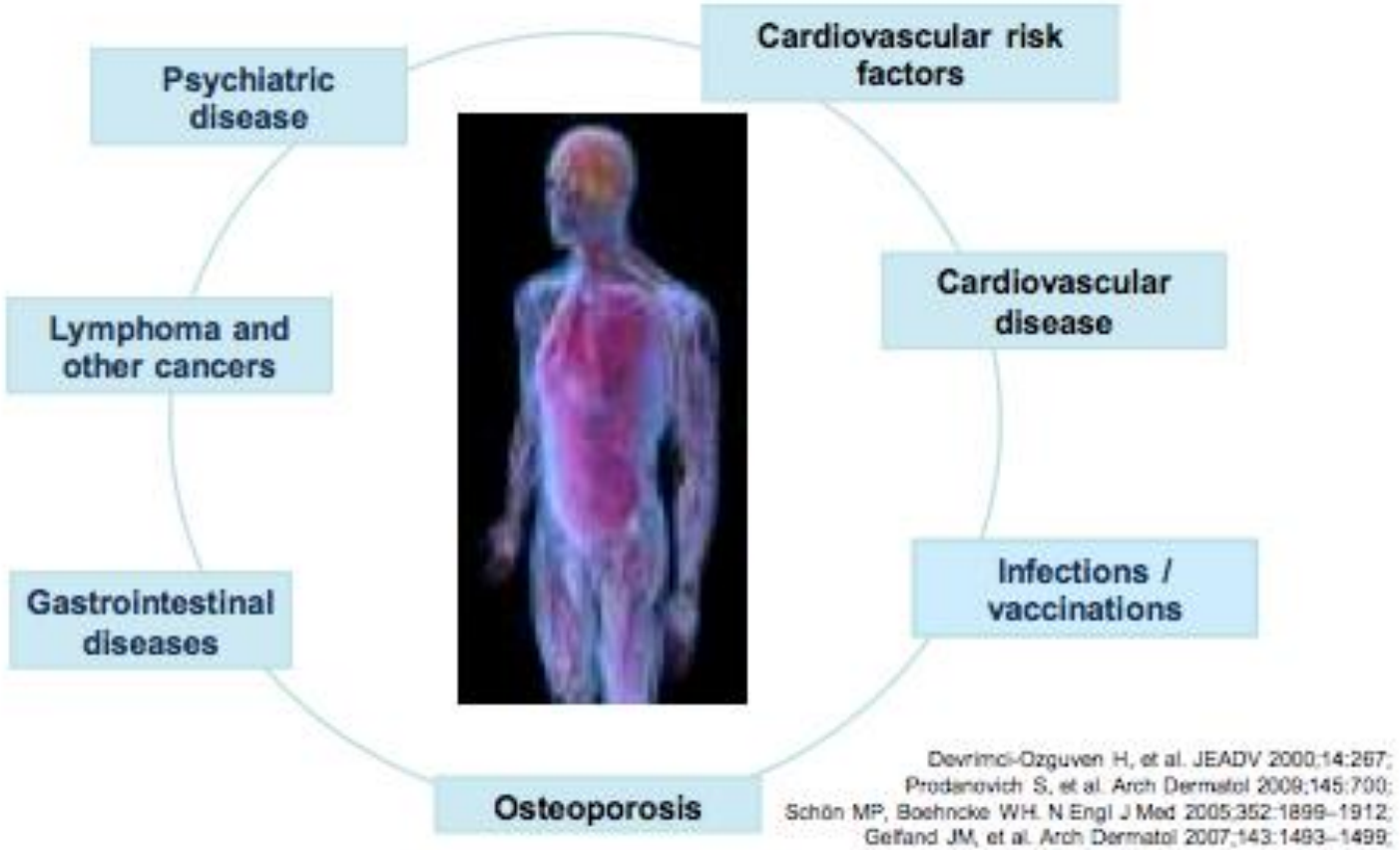
- “Comorbidity” describes medical conditions that exist at the time of diagnosis of the index disease, but are not necessarily a consequence of that index disease

- “Multi-morbidity” usually defined as when an individual has two or more long-term conditions- ie: the co-occurrence of medical conditions within a person

In clinical practice comorbidity and multimorbidity are:

- *underrecognized, under- diagnosed, underestimated and undertreated.*

The range of multi(co)morbidities in RA...



Devrimci-Ozguven H, et al. JEADV 2000;14:267;
Prodanovich S, et al. Arch Dermatol 2009;145:700;
Schön MP, Boehncke WH. N Engl J Med 2005;352:1899–1912;
Gelfand JM, et al. Arch Dermatol 2007;143:1493–1499;
Gelfand JM, et al. Infect Dis 2006;126:2194

Clinical Impact- Multimorbidity associated with:

- *reduced quality of life*
- *higher mortality*
- *reduced socioeconomic status*
- *poly-pharmacy*
- *high treatment burden*
- *higher rates of adverse drug events*
- *greater health services use including emergency hospital admission*

nature REVIEWS RHEUMATOLOGY

Radner et al, 2014

Prevalence of Multimorbidities

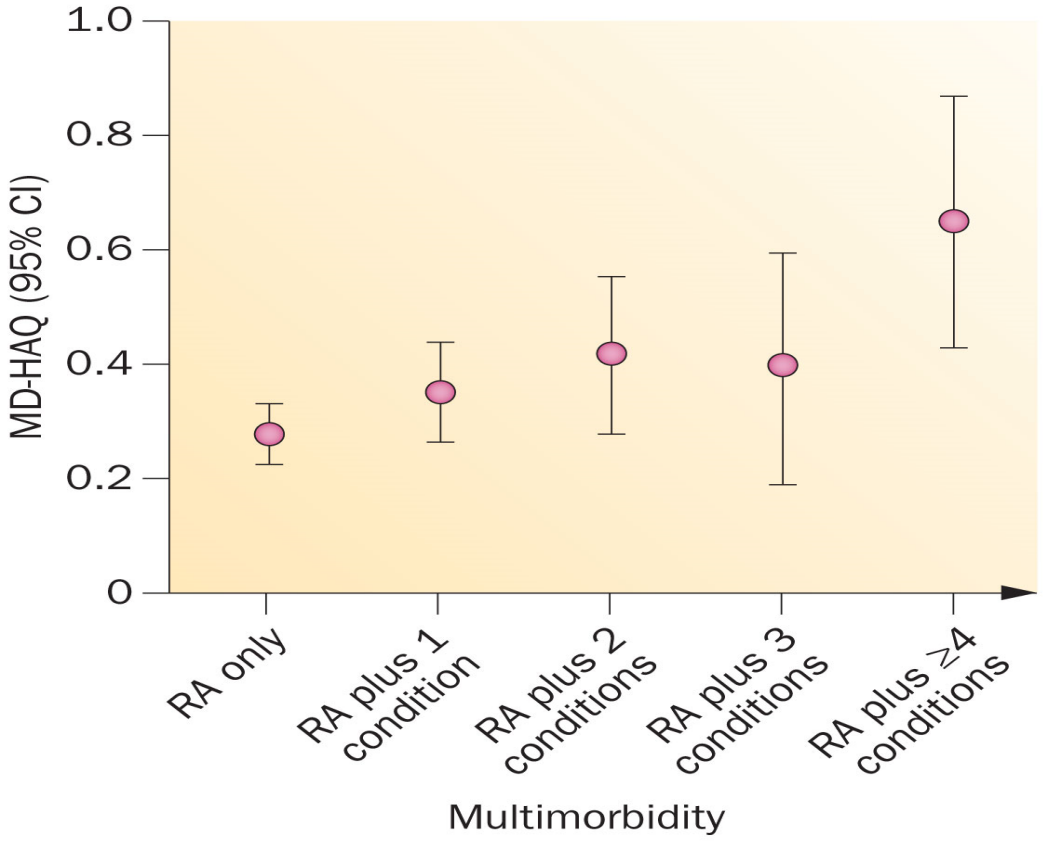
- Radner, Wien Klin Wochenschr (2016) 128:786–790

Table 1 Prevalence of different morbid conditions in inflammatory rheumatic conditions

Morbid conditions	RA (%) [8, 50]	SpA (%) [51]	SLE (%) [18, 52–56]
Cardiovascular disease	6	3	6–10
Cardiovascular risk factors			
Hypertension	40	34	40
Dyslipidemia	32	27	36–60
Diabetes	14	9	11
Osteoporosis	30	13	23
Cancer (any solid)	5	3	3.2
Depression	15	11	46

RA rheumatoid arthritis, *SLE* systemic lupus erythematosus, *SpA* spondylarthropathies

The impact of multimorbidity on physical function in a cohort of 282 patients with RA who reached the target clinical disease activity index <10



nature REVIEWS RHEUMATOLOGY

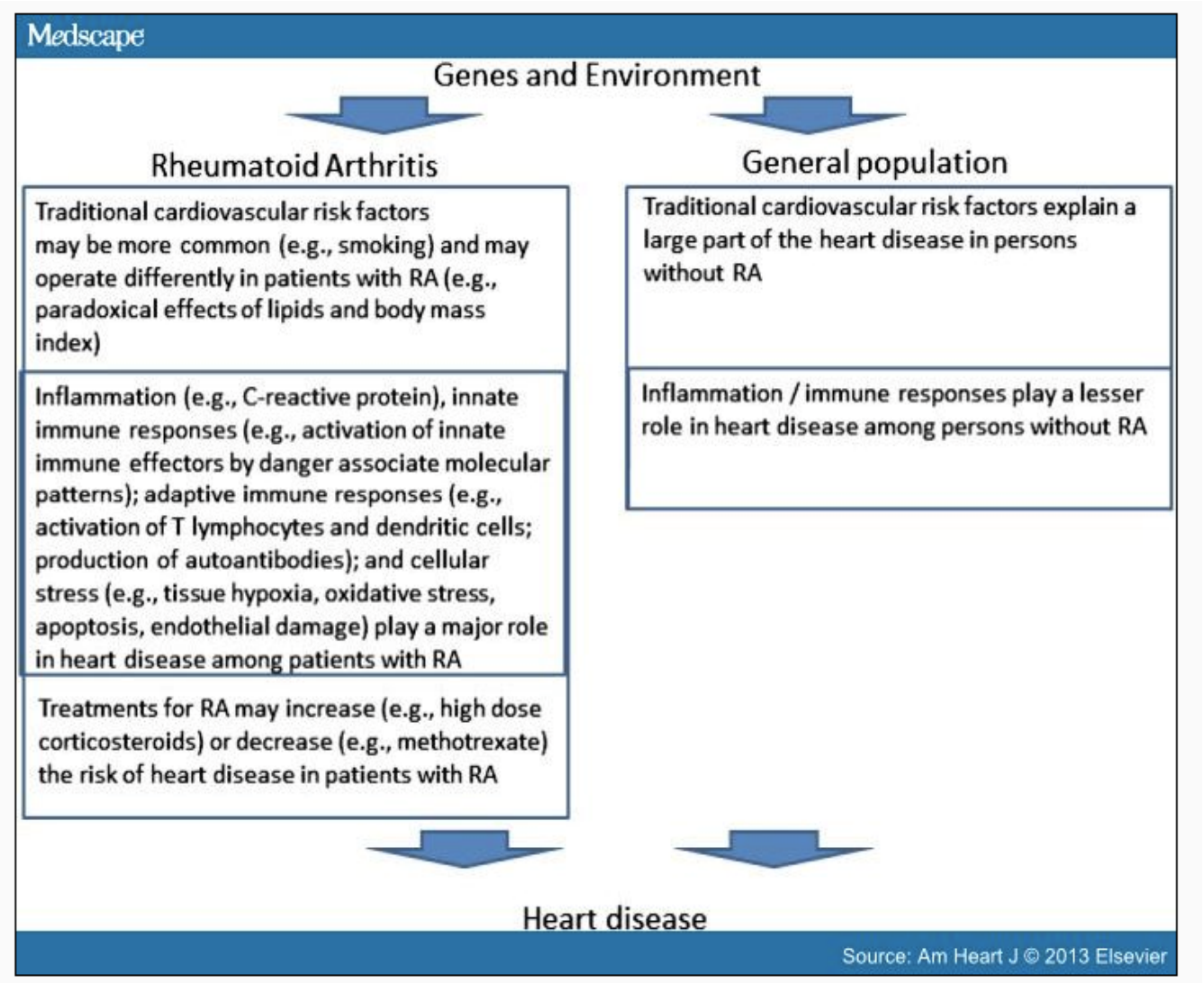
NICE: The Multidisciplinary Team

- People with RA should have ongoing access to a multidisciplinary team. This should provide the opportunity for periodic assessments of the effects of the disease on their lives* and help to manage the condition.

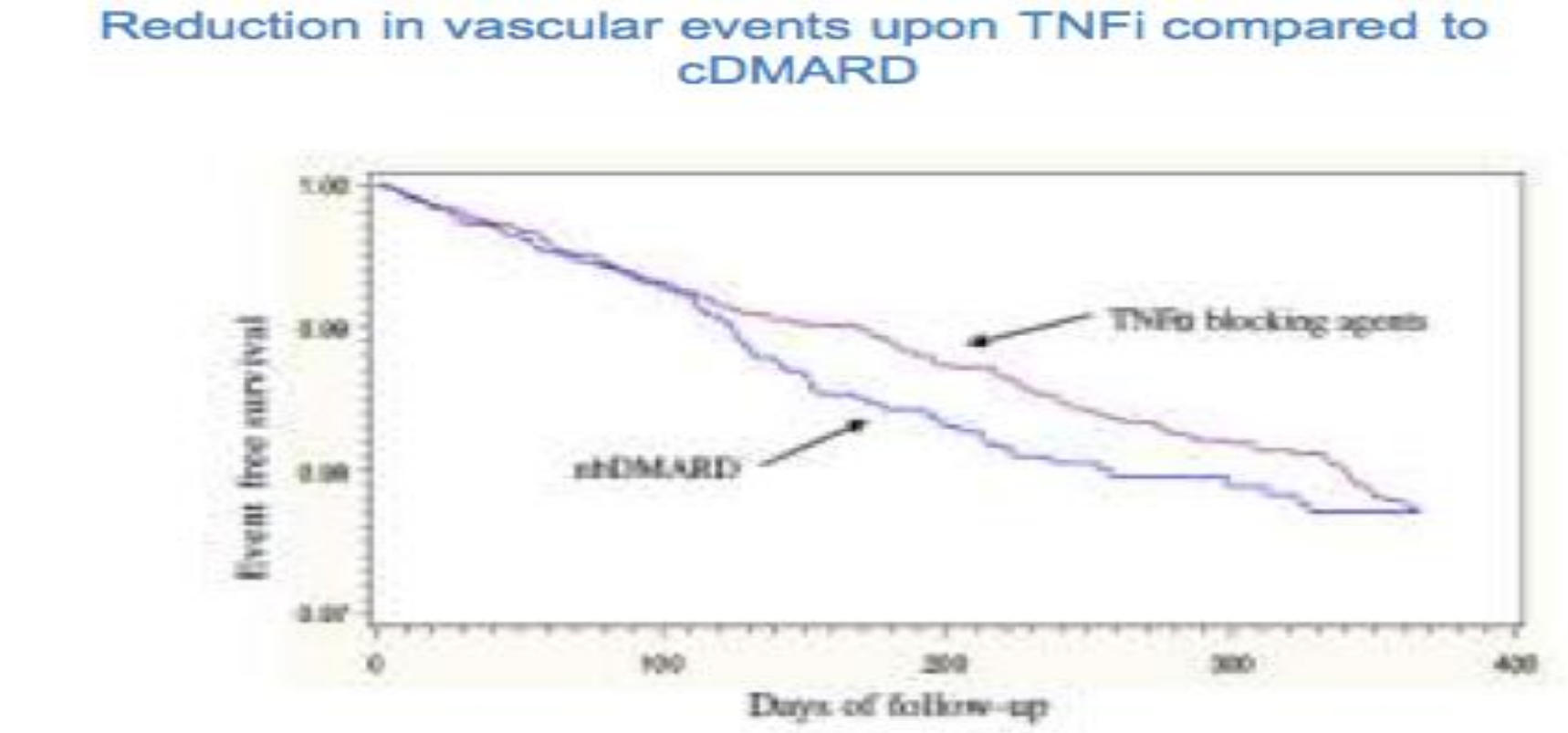
* (such as pain, fatigue, everyday activities, mobility, ability to work or take part in social or leisure activities, quality of life, mood, impact on sexual relationship)

NICE Guidelines, 2016

Why do patients with RA develop heart disease?



Anti-TNF Reduce events:
Event free survival with Tx



Solomon DH et al. *Am J Med* 2013;126;730.

EULAR 2015 recommendation update for cardiovascular risk management in patients with rheumatoid arthritis…

	Recommendations 2015	Level of evidence	Voting (0-10)
6	CV risk score models should be adapted for patients with RA by a 1.5 multiplication factor, if this is not already included in the score.	3-4, C-D	
7	CV risk management should be carried out according to national guidelines in RA, AS or PsA. Antihypertensives and statins may be used as in the general population.	3-4, C-D	
8	Prescription of NSAIDs in RA and PsA should be with caution, especially for patients with a documented CV disease or in the presence of CV risk factors. NSAIDs are recommended as first-line drug treatment for AS patients with pain and stiffness (unless contra-indicated).	2A-3C-D	
9	Corticosteroids: for prolonged treatment, the glucocorticoid dosage should be kept to a minimum, and a glucocorticoid taper should be attempted in case of remission or low disease activity; the reasons to continue glucocorticoid therapy should be regularly checked.	3C	
10	Life style recommendations should emphasise the benefits of a healthy diet, regular exercise and smoking cessation.	4D, 3C, 1B	

Nurmohamed M, et al. EULAR 2015 SP0033
June 10, 2015, 17:00–18:30 Hot Topics Session 2: EULAR recommendation update on cardiovascular disease in RA

RA clinical assessment & management: What should be done

- **Measure BP**
- **Non-fasting lipids to get TC and HDL-c**

  (TC and HDL-c same fasting vs non- fasting)
- **Ask re: smoking status**
- **Assess BMI**
- **Risk factor calculation-**

  National preferred tools recommended

  EULAR : SCORE plus multiplication factor x 1.5

Is There a Care Gap in Inflammatory Arthritis (IA)?

- Explosion of new meds for IA- DMARDS, Biologics, targeted oral small molecules…..
- Outcomes are overall better, and we have many more Tx options
- However, our target is not just symptom relief, but now it is “remission ”
- Despite all our new available drugs, rates of remission are still only about 30-35% in most clinical trials
- Meds have toxicities, particularly increased infections

What Do We Hear From Our Patients?

- The drugs we offer are frightening- “immune suppressive”, “chemotherapy”….
- “I’m not a drug person”
- Is there a diet for arthritis?
- Are there “natural” products I can take?

- Bottom line:

  Patients want to be heard, and validated, and we have a responsibility to listen to them,guide them, and partner with them.

  Essentially every new guideline starts with an overarching principle of “shared decision making” with our patients. This will enhance compliance and adherence.

Impact of Diet

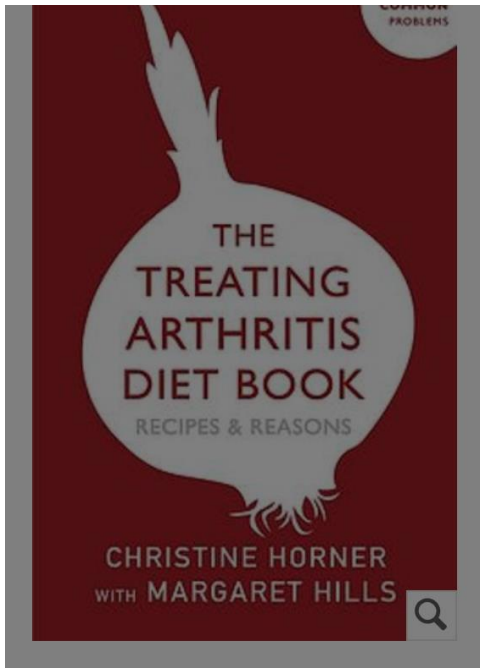
No specific diet for arthritis

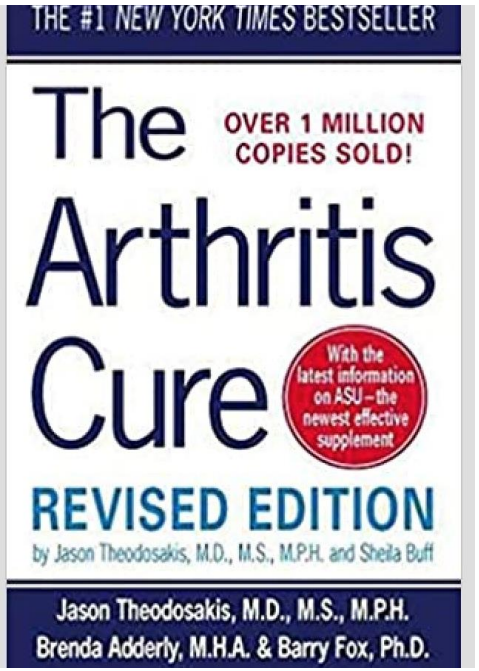
- No “one size fits all” diet
- Many studies often with conflicting and non reproducible results
- Many books, lots of internet misinformation
- There are some reasonable “do’s and dont’s”, and some science
- Credible info available from sources such as ACR, EULAR, CRA, TAS etc…

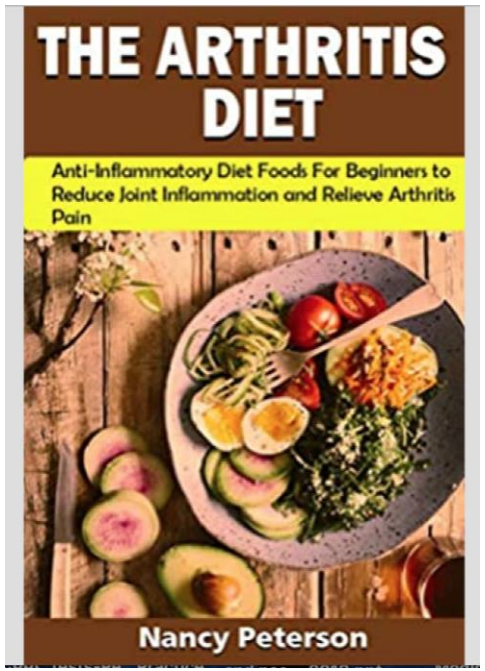
But, diets are hard to study

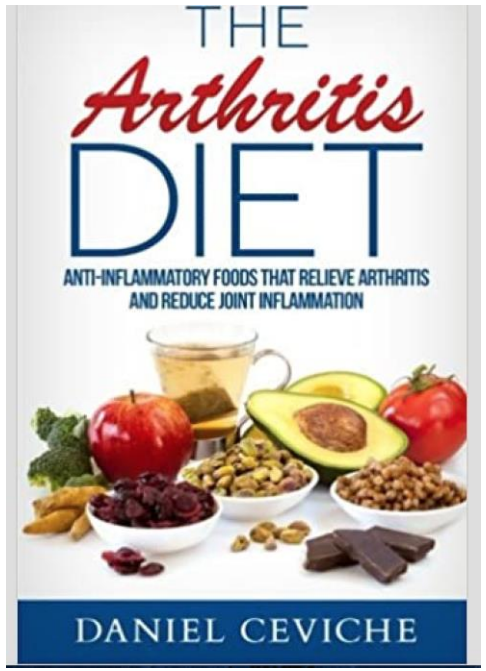
- Hard to control
- Placebo effect
- Compliance
- Comorbidities, confounders

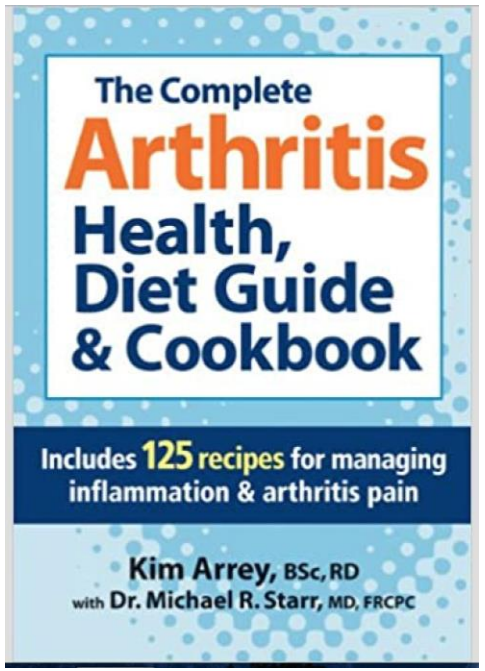
Many Arthritis Diet Books available: How to choose?











Impact of Anti-inflammatory Diet

- Study: Active RA, 2 weeks anti-inflammatory diet

  The “ITIS” diet significantly improved fatigue in RA patients, and was associated with changes in the fecal microbiome and metabolomics. Reduced ESR, but not CRP

  Coras R, ACR abstract 1699, Nov 2021

- Cross sectional analysis of eating fresh fish twice a week reduced DAS28-CRP disease activity measure in RA patients

  Tedeschi SK, Arthritis Care Res. 2018 Mar.70:327-332

- Effect of intermittent fasting- reduced inflammation (CRP), increased apoptosis of autoimmune cells- may have benefits in RA and PsA. Hard to maintain though.

  Aliki I, Medit J Rheumatol, 2019 Dec;30(4):201-206. Lit. review

What is Sensible Diet Advice to Give to Our Patients?

- Generally, follow a Mediterranean style diet high in fish, whole grains, nuts, fruits, vegetables
- Limit processed foods, red meats, sugary snacks
- Cook with olive oil
- Avoid “high heat” cooking
- Consider reducing nite shades ,and gluten, and maybe dairy to determine if you are sensitive to these foods
- If you consider elimination diet, especially dairy, eat foods with calcium and other nutrients to replace it →kale, almonds, soy, eggs…

Impact of Obesity and Weight Loss

- Obesity can increase inflammation, increase CRP (George M, Arth Care Res. April,2017)
- As little as 10 lb weight loss can decrease progression of knee OA (Bliddel et al, Obes Rev 204, July; 15(7): 578-586)
- Initial goal should be weight loss of 10%
- High BMI patients- mean change in outcome measures on biologics in Psoriatic Arthritis lowest for overweight and obese patients (Purcell E, ACR abstract 1327, Nov 2021)
- Obesity related to higher disease burden and labour loss in Spondyloarthritis patients (Duruoz M, ACR abstract 1320, Nov 2021)
- Adipokines may influence the progression of RA, and erosive disease (Meyer M, Arthritis Rheumatol. 2013;15:R210)

Smoking

- Increases citrullination of proteins in lungs
- Increased risk of getting disease
- Impact on CV comorbidity in patients already at risk
- Poorer prognosis and outcomes
- Poorer response to biologics
- Imperative that smoking cessation be a part of managing patients with IA !

RA associated with increased risk of infection

- **Inflammatory diseases *per se***

  Immune senescence ,
  Immune dysregulation

- ***Therapeutics***

  Glucocorticoids especially in higher doses

  bDMARDs, tsDMARDs

- ***Co-morbidities***

  Cigarette smoking

  Diabetes

RA and Vaccines

Live	Not-live
BCG	Anthrax
Influenza (nasal)	Hepatitis A
Mumps/Measles/Rubella	**Hepatitis B**
Polio (oral)	**Influenza (IM)**
Rotavirus	*H. influenzae*
Shingles	HPV
Smallpox	Japanese Encephalitis
Varicella	Meningococcal
Yellow Fever	**Pneumococcal**
Typhoid (oral)	Poliomyelitis (IM)
	Rabies
	Tetanus/diptheria/pertussis (Td/Tdap)
	Typhoid (IM)

DMARDS and Vaccine Immunogenicity

	MTX	TNFi	ABA	RTX	TOC	TOFA
Influenza	+/-	OK	+/-	↓	OK	OK
PPSV-23 (Pneumovax®)	↓	+/-	+/-	↓	OK	↓
Zoster	?	?	?	?	?	?
Tetanus			OK	OK	OK	

Recall: vaccine efficacy is commonly measured by elevation (change from baseline or booster) in antibody titre, rarely by impact on infectious event rate

What about Covid vaccines?

Malignancy and RA:
The clinical challenges

- RA *itself carries increased risk of lymphoma and some solid tumors (ex: lung)….so screen carefully at baseline*

- *No increased risks from Biologics for most tumors (especially solid tumors); outcomes if onset during therapy seem to be equivalent.*

  Caution however with melanoma

- *Risks imposed by prior malignancy→ more data needed*

Clinical Dilemma: Prior Malignancy

- Ensure oncologist is informed and in partnership
  - Optimize tumor therapeutics
  - Capture RA disease suppression
  - Reassure that all aspects of their health are being considered
- Optimize use of DMARDS - Consider combination
  - Glucocorticoids
  - Moderate T-2-T strategy- manage expectations
- Choose biologic if necessary
  - Rituximab if <5yrs preferred
  - General choice of MOA >5yrs
  - Except melanoma (no TNFi)

Mental Health in Inflammatory Arthritis

- Depression common in IA (about 20% by most estimates), and depression reduces odds of treatment response by >30% in RA
- Possibly shared pathophysiological mechanisms; inflammatory cytokines linked to depression
- Depression and anxiety reduce the chance of remission in RA (https://doi.org/10.1136/annrheumdis-2017-211284
- Immune modulating therapy shown to decrease not only disease activity but also comorbidities including depression
- Mindfulness based stress reduction improved anxiety, depression and function in RA (Boire G, ACR abstract 1244, Nov 2021)
- Multidisciplinary approach to include mental health professionals in management of IA seems relevant

Nerurkar L, Lancet Psychiatry S2215-0366(18)30255-4, Oct 23, 2018;
Matcham, F, Rheumatology, 2018;57(5):835-843

RA Disease Factors Related to Depression

Inflammation

- Systemic inflammation may be associated with, cause, or contribute to depressive symptoms
- Acute phase reactants and pro-inflammatory cytokines are often associated with depression
- Elevated cytokines in major depression- e.g., IL-1, IL-6 and TNF
- Inflammation may cause treatment resistance to anti-depressants

RA and Depression: Approach

- First need to be aware of the problem !
- Beware the disconnect between patient and doctor global assessment!
- Explain “reactive” vs “intrinsic” effect on mood state mediated by RA
- Screen if indicated , Depression scales (PHQ-9, BDI-II, GAD-7)
- Treat in partnership with psychiatric or primary care services & family when possible

RA and Depression

- Encourage patients to continue doing the things they find enjoyable in life
- Encourage use of credible information sources (e.g., Arthritis Society, RheumInfo, US, UK sites)
- Validate patient feelings
- Encourage optimisim:
  - "There has never been a better time to have RA"
  - A happy, productive life is possible in RA

2022 American College of Rheumatology (ACR) Guideline for Exercise, Rehabilitation, Diet, and Additional Integrative Interventions for Rheumatoid Arthritis

Guideline Summary

Table 1. Recommendations on integrative interventions for the management of rheumatoid arthritis (RA)

Exercise	Rehabilitation	Diet	Additional
Consistent engagement in exercise (++)	Comprehensive occupational therapy (+)	Mediterranean-style diet (+)	Standardized self-management program (+)
Aerobic exercise (+)	Comprehensive physical therapy (+)	Against formally defined diet other than Mediterranean-style (-)	Cognitive behavioral therapy and/or mind-body approaches (+)
Aquatic exercise (+)	Hand therapy exercises (+)	Against dietary supplements (-)	Acupuncture (+)
Resistance exercise (+)	Splinting, orthoses, compression, bracing, and/or taping (+)		Massage therapy (+)
Mind-body exercise (+)	Joint protection techniques (+)		Thermal modalities (+)
	Assistive devices, adaptive equipment, and/or environmental adaptations (+)		Against electrotherapy (-)
	Vocational rehabilitation, work site evaluations and/or modifications (+)		Against chiropractic therapy (-)

Strong recommendations **for** an intervention are shown in dark green and ++.
Conditional recommendations **for** an intervention are shown in light green and +.
Conditional recommendations **against** an intervention are shown in light red and -.

This summary was approved by the ACR Board of Directors on October 31, 2022. These recommendations are included in a full manuscript, which will be submitted for publication in Arthritis & Rheumatology and Arthritis Care and Research.

ACR Abstract, Nov.,2022

Take Away Messages:
Value of Treating the Whole Patient

- In patients with chronic inflammatory rheumatic conditions, multimorbidity is highly prevalent with an impact on important clinical outcomes such as disease activity, physical function, or mortality.
- Multimorbidities and lifestyle choices need to be considered in managing the “whole” patient with IA
- Patients want to have advice and choice on alternate treatment options aside from pharmacotherapy
- Treat co-morbid conditions in concert- excellent opportunity where collaborative care can make a difference!

Sir William Osler:

"The Good Physician Treats the Disease; The Great Physician Treats the Patient Who Has the Disease"


danke
謝謝
teşekkür ederim
спасибо
thank you
gracias
dank je
dziękuję
go raibh maith agat
mochchakkeram
obrigado
sukriya
kop khun krap
grazie
arigatō
dakujem
terima kasih
merci
мерси
감사합니다
blagodaram
faafetai lava
hvala
tack
mersi
barka
paldies
matondo
misaotra
djiere dieuf
asante
хвала
trugarez
shukriya
dhanyavadagalu
diolch
xiexie
rahmet
tanemirt
najis tuke
sagolun
mesi
dekuji
sobodi
enkosi
chnorakaloutioun
gracies
suipay
dankie
kiitos
Баярлалаа