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ΚΑΘΗΜΕΡΙΝΗΣ ΚΛΙΝΙΚΗΣ ΠΡΑΞΗΣ

Λοιμώξεις σε ασθενείς με συστηματικά αυτοάνοσα νοσήματα

Δημήτριος Α. Βασιλόπουλος
Κοινό Πρόγραμμα Ρευματολογίας
Μονάδα Κλινικής Ανοσολογίας-Ρευματολογίας
Β' Παθολογική Κλινική και Ομώνυμο Εργαστήριο
Ιατρική Σχολή ΕΚΠΑ
Ιπποκράτειο ΓΝΑ

Conflicts of interest

Research grants (through ELKE)	Other research support	Honoraria/ advisory board fees
Abbvie	Special Account for Research Grants, University of Athens (ELKE)	Abbvie
Genesis - Pharma	Hellenic Society for Rheumatology (ERE-EPERE)	Actelion
MSD		Bristol-Myers Squibb
Novartis		Janssen
Pfizer		MSD
Roche		Novartis
UCB		Pfizer
		Roche
		UCB

None relevant to this presentation

Dimitrios Vassilopoulos, MD

Outline

- Viral infections (HBV, HCV, Chikungunya virus)
- Vaccinations
- Tuberculosis
- Serious infections in RA
- Serious infections in SLE

Hepatitis B and C in RA: How common?

EXTENDED REPORT

Prevalence of comorbidities in rheumatoid arthritis and evaluation of their monitoring: results of an international, cross-sectional study (COMORA)

Maxime Dougados,[1,2] Martin Soubrier,[3] Anna Antunez,[4] Peter Balint,[5] Alejandro Balsa,[6] Maya H Buch,[7,8] Gustavo Casado,[9] Jacqueline Detert,[10] Bassel El-zorkany,[11] Paul Emery,[7,8] Najia Hajjaj-Hassouni,[12] Masayoshi Harigai,[13] Shue-Fen Luo,[14] Reka Kurucz,[5] Gabriel Maciel,[15] Emilio Martin Mola,[16] Carlo Maurizio Montecucco,[17] Iain McInnes,[18] Helga Radner,[19] Josef S Smolen,[19] Yeong-Wook Song,[20] Harald Erwin Vonkeman,[21] Kevin Winthrop,[22] Jonathan Kay[23]

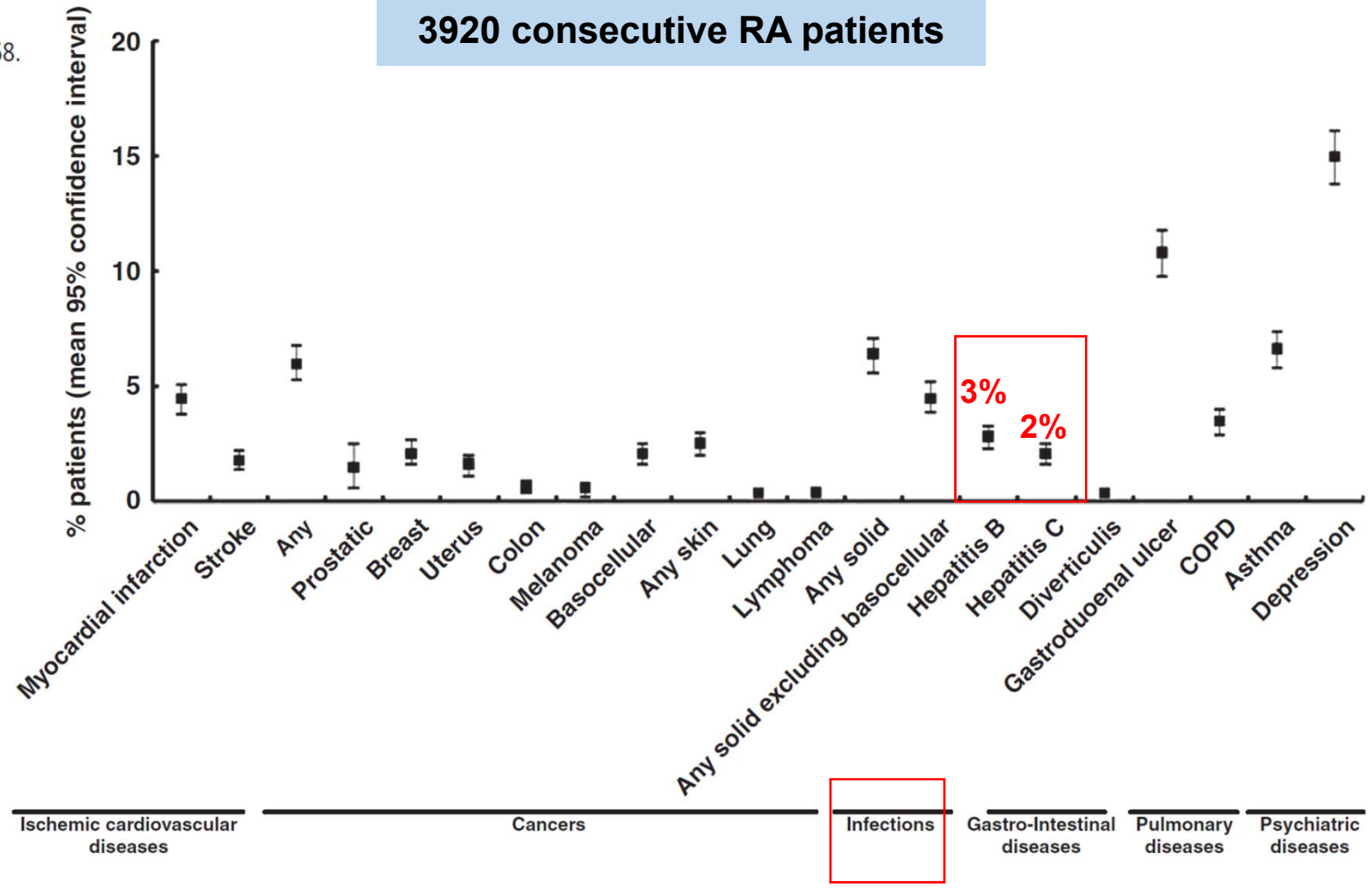
Dougados M, *et al*. *Ann Rheum Dis* 2014;**73**:62–68.

Cross-sectional, observational, multi-center, international study (COMORA Study)

17 centers

3920 consecutive RA patients

Country	Number of patients
Argentina	200
Austria	204
Egypt	308
France	411
Germany	209
Hungary	201
Italy	228
Japan	207
Korea	400
Morocco	227
Netherlands	139
Spain	200
Taiwan	313
UK	43
Uruguay	30
USA	400
Venezuela	200
Total	**3920**



Hepatitis B and C in AS: How common?

EXTENDED REPORT

Prevalence of comorbidities and evaluation of their screening in spondyloarthritis: results of the international cross-sectional ASAS-COMOSPA study

Anna Moltó,[1,2] Adrien Etcheto,[1,2] Désirée van der Heijde,[3] Robert Landewé,[4] Filip van den Bosch,[5] Wilson Bautista Molano,[6] Ruben Burgos-Vargas,[7] Peter P Cheung,[8] Eduardo Collantes-Estevez,[9] Atul Deodhar,[10] Bassel El-Zorkany,[11] Shandor Erdes,[12] Jieruo Gu,[13] Najia Hajjaj-Hassouni,[14,15] Uta Kiltz,[16] Tae-Hwan Kim,[17] Mitsumasa Kishimoto,[18] Shue-Fen Luo,[19] Pedro M Machado,[20,21] Walter P Maksymowych,[22] José Maldonado-Cocco,[23] Helena Marzo-Ortega,[24] Carlo-Maurizio Montecucco,[25] Salih Ozgocmen,[26] Floris van Gaalen,[3] Maxime Dougados[1,2]

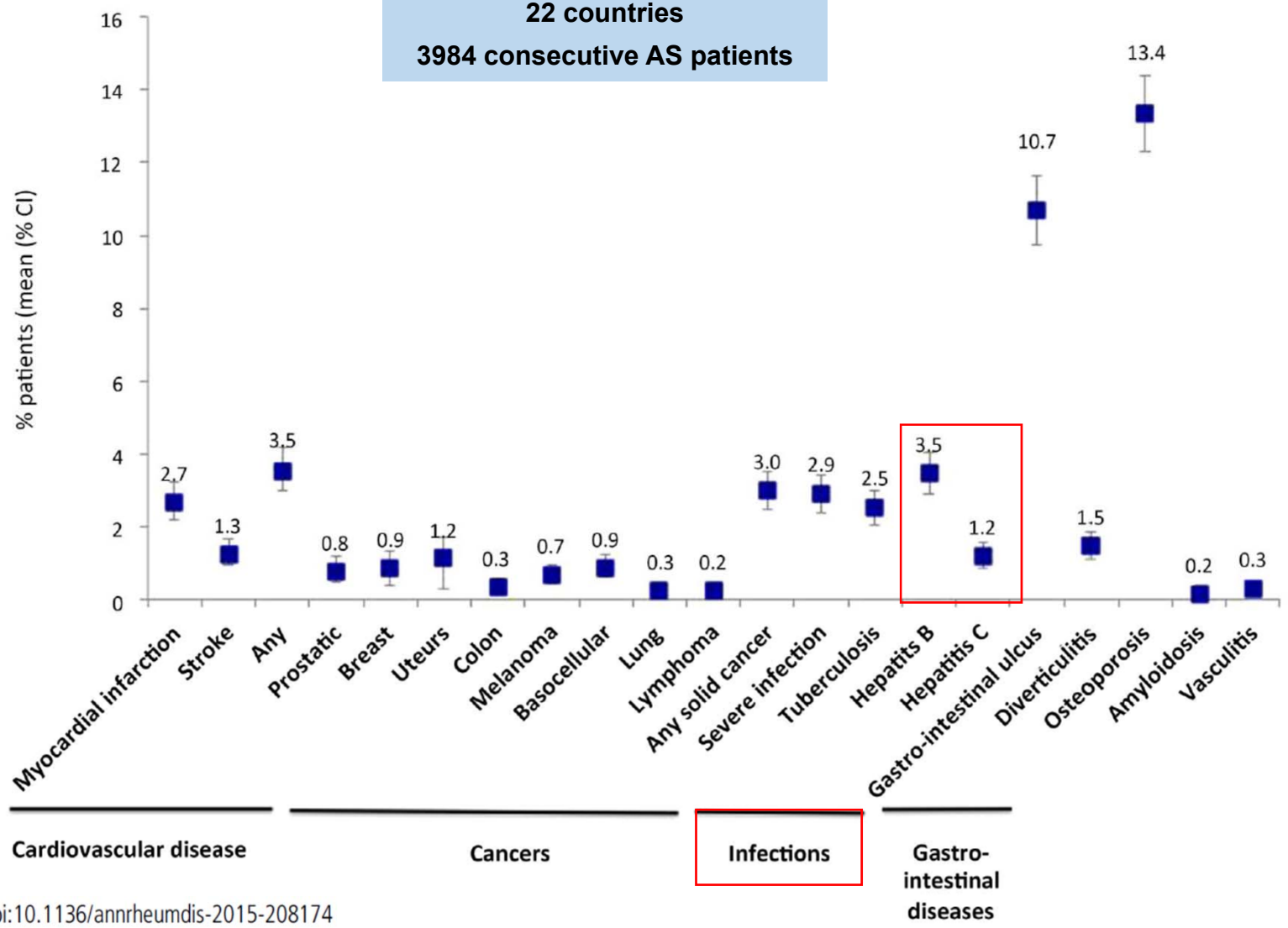
Country	Number of patients
Argentina	236
Belgium	50
Canada	41
China	248
Colombia	47
Egypt	224
France	337
Germany	198
Italy	200
Japan	161
Mexico	69
Morocco	113
Netherlands	200
Portugal	92
Russia	192
Singapore	206
South Korea	238
Spain	232
Taiwan	241
Turkey	254
UK	204
USA	201
Total	**3984**

Cross-sectional, observational, multi-center, international study (COMORA-AS Study)

22 countries

3984 consecutive AS patients

Age = 44 yrs
♂ = 65%
Dis. duration = 8 yrs



Ann Rheum Dis 2015;**0**:1–8. doi:10.1136/annrheumdis-2015-208174

What is the risk for reactivation in patients with past HBV infection treated with biologics?

HBV

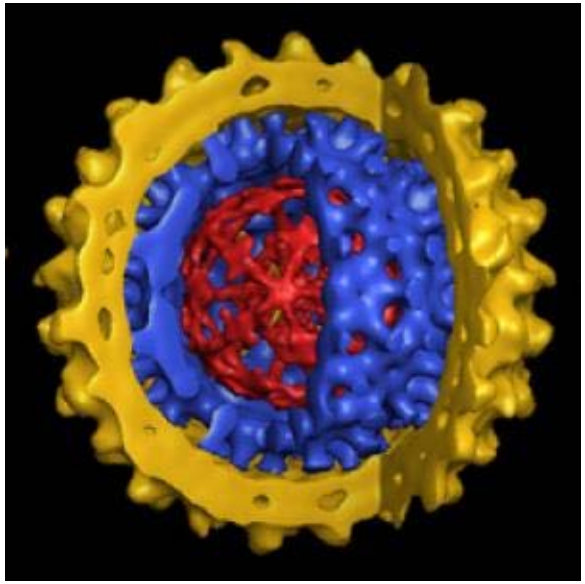


Image courtesy of Scripps Research Institute

- **Worldwide: Past HBV infection (5-80%)**

  (HBsAg-/antiHBc+)

- **In hematologic disease (lymphomas):**

  RTX-regimens lead to reactivation in 3-25% of past HBV infection

- **Need for pre-emptive antiviral prophylaxis??**

- **There are limited data in rheumatic pts treated with rituximab or other biologics**

Risk of reactivation in patients with past HBV infection treated with biologics

Safety of Long-Term Biologic Therapy in Rheumatologic Patients With a Previously Resolved Hepatitis B Viral Infection

Michele Barone,[1] Antonella Notarnicola,[2] Giuseppe Lopalco,[2] Maria Teresa Viggiani,[3] Francesco Sebastiani,[3] Michele Covelli,[2] Florenzo Iannone,[2] Alfonso W. Avolio,[4] Alfredo Di Leo,[3] Luca Cantarini,[5] and Giovanni Lapadula[2]

Italy

n=1218 rheumatic pts
treated with biologics (2001-2012)

→ HBsAg+
n=41 (3%)

↓

n=179 (15%)
with past HBV infection
(HBsAg-/anti-HBc+)

↓

Anti-HBs+
80%

Anti-HBs-
20%

↓

Treated with:

- Rituximab	n=14
- Anti-TNF	n=146
- Other biologics	n=19
Tocilizumab	*n=7*
Abatacept	*n=7*
Anakinra	*n=3*

Barone M et al, Hepatology 2015

Risk of reactivation in rheumatic patients with past HBV infection treated with biologics

- **No cases** of HBV reactivation during biologic Rx

- **9%** (17/179): ↑ **ALT** levels (14/19: < 2x ULN, 3/19: > 2x ULN)

	Anti-HBs levels
RTX	↓10%
Anti-TNF	↓ 8%
Other biologics	↓ 9%

Barone M et al, Hepatology 2015

-These findings, confirm results from previous studies, showing that the risk for HBV reactivation in rheumatic patients with past HBV infection treated with anti-TNFs[1-3] or rituximab[4] is very low

- No need for prophylactic antiviral treatment

[1] *Vassilopoulos D et al, Ann Rheum Dis 2010*
[2] *Caporalli R et al, Arthritis Care Res 2010*
[3] *Charpin C et al, Arthritis Res Ther 2009*
[4] *Mitroulis I et al, Ann Rheum Dis 2013*

HCV infection: What do we need to know?

HCV

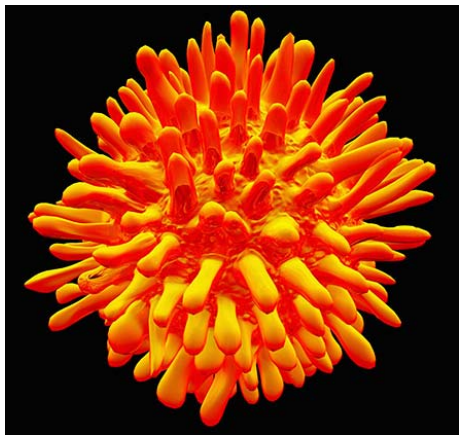
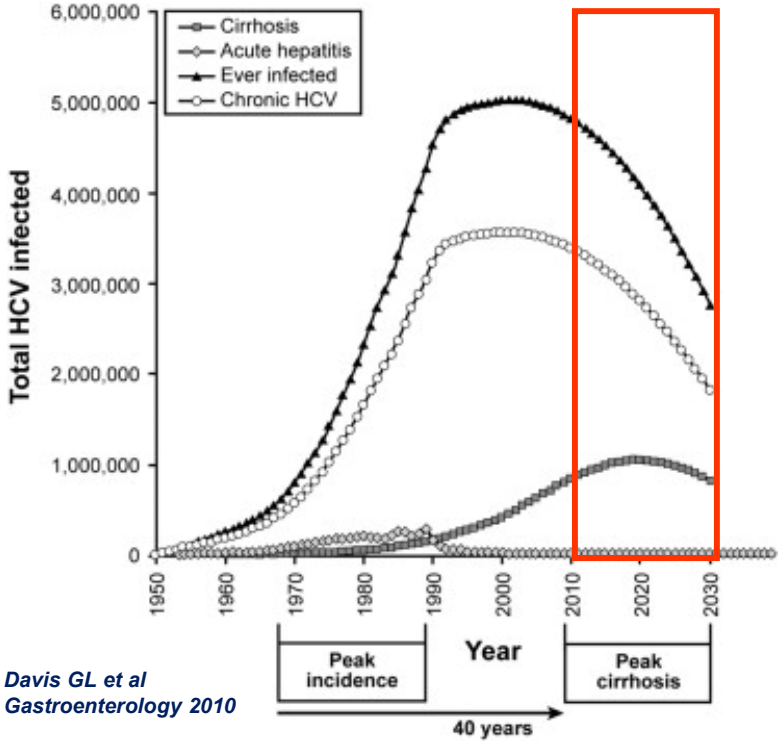


Image courtesy of Science Photo Library



Davis GL et al Gastroenterology 2010

- Worldwide health problem (2.8%)
- Universal screening between 45-65 yrs recommended *(CDC)*
- Associated with potentially serious rheumatic complications like HCV-associated cryoglobulinemic vasculitis (CV)
- Interferon (IFNa) schemes achieve viral clearance in ~50%
- INFa: Common side effects (cytopenias, depression, flu-like symptoms) and contraindications (↓↓ CrCl)
- New oral Direct Acting Antivirals (DAAs) are being introduced in clinical practice

HCV infection: New DAAs

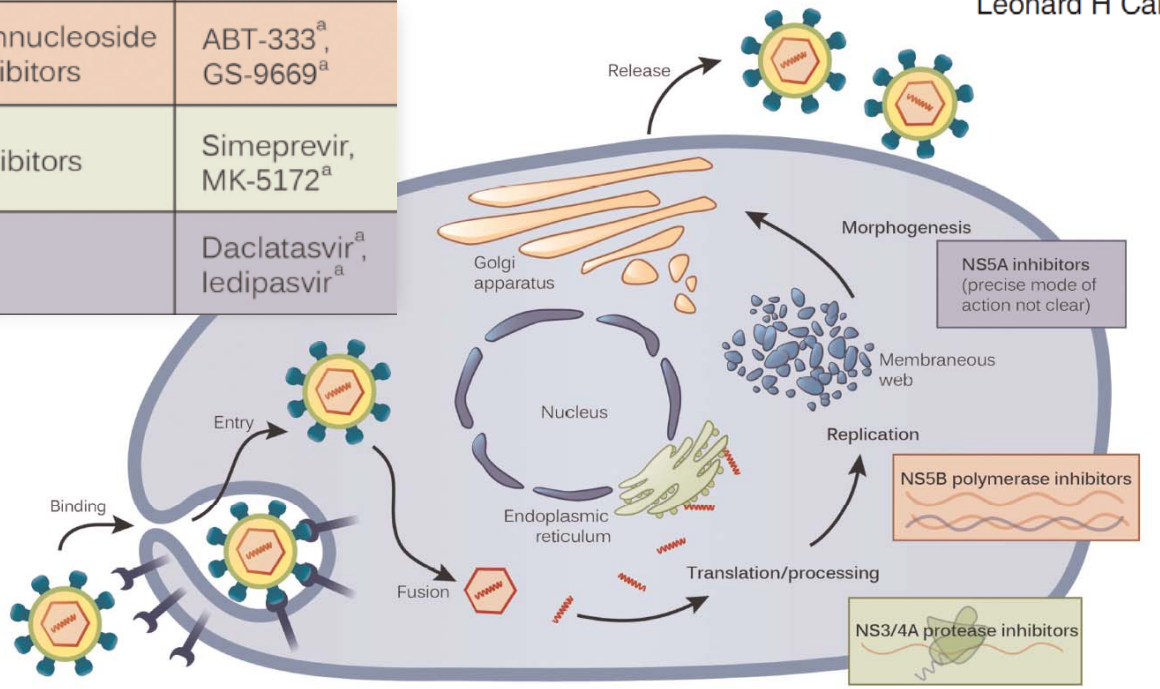
DAA Drug Class		Examples
Nonstructural protein (NS)3b polymerase inhibitors	Nucleos(t)ide inhibitors	Sofosbuvir
	Nonnucleoside inihibitors	ABT-333[a], GS-9669[a]
NS3/4A protease inhibitors		Simeprevir, MK-5172[a]
NS5A inhibitors		Daclatasvir[a], ledipasvir[a]

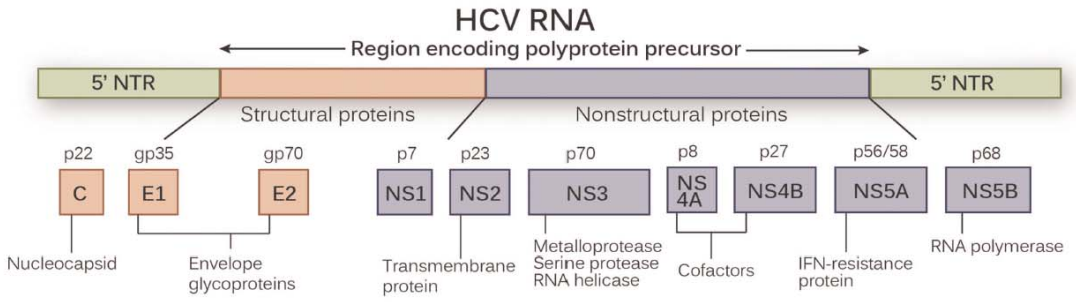
RMD Open
Rheumatic & Musculoskeletal Diseases

VIEWPOINT

For patients with rheumatic disease and hepatitis C infection: the end of interferon

Leonard H Calabrese,[1] Patrice P Cacoub[2,3,4,5]

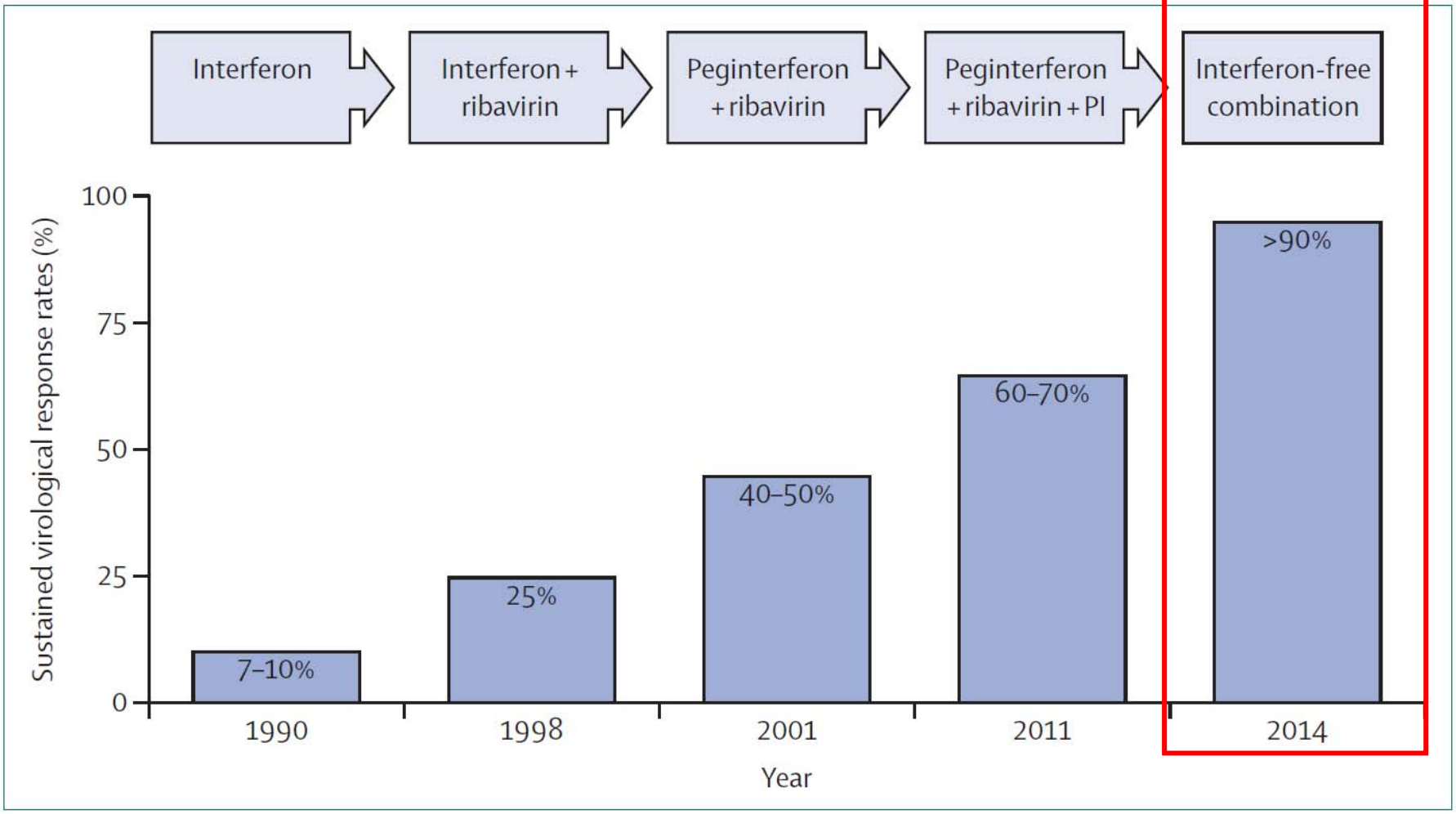




RMD Open 2015

DAAs: Oral IFN-free regimens

Closer to the cure (>90%)



Webster DP et al, Lancet 2015

DAAs: Cost issues

MEDICINE

Hepatitis C can be cured globally, but at what cost?

New drugs to cure hepatitis C should be made available at low costs in developing countries

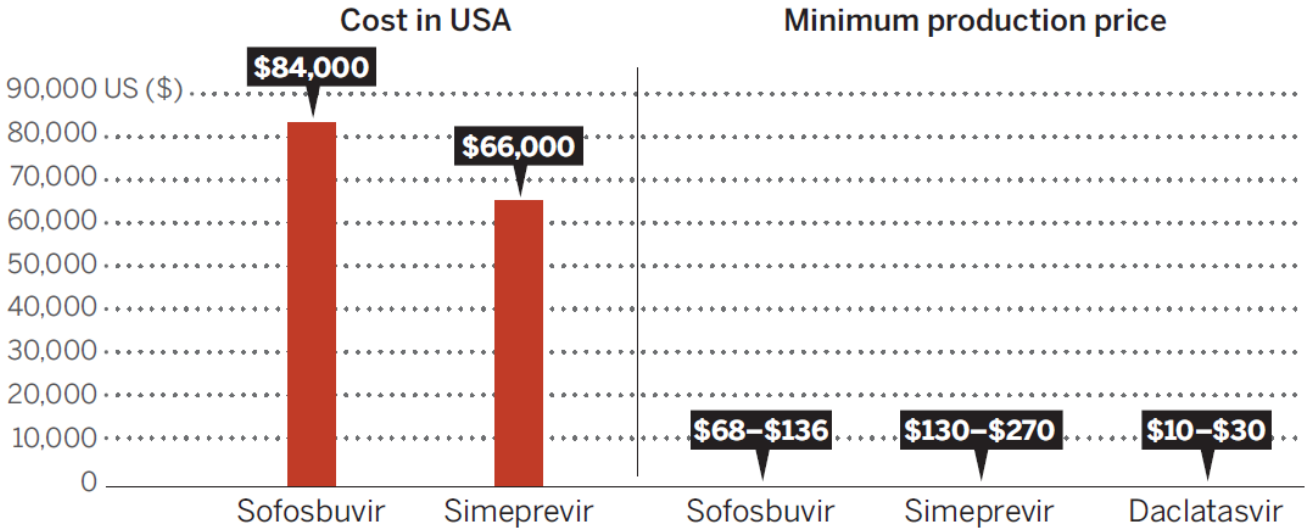
SCIENCE

11 JULY 2014 • VOL 345 ISSUE 6193

By **Andrew Hill**[1] *and* **Graham Cooke**[2]

Costs of new drugs for hepatitis C per person, 12-week course

New generation drugs for HCV



Sofosbuvir (12 wk course)

Germany	**$75,000**
France	**$70,000**
Canada/UK	**$55,000**

http://esofosbuvir.com/sofosbuvir-drug/sofosbuvir-cost/

HCV-associated cryoglobulinemic vasculitis: A therapeutic priority

American Association for the Study of Liver Diseases — AASLD

Recommendations for Testing, Managing, and Treating Hepatitis C

IDSA Infectious Diseases Society of America

When and in Whom to Initiate HCV Therapy Table 1. Settings of Liver-Related Complications and Extrahepatic Disease in Which HCV Treatment is Most Likely to Provide the Most Immediate and Impactful Benefits

Highest Priority for Treatment Owing to Highest Risk for Severe Complications

Advanced fibrosis (Metavir F3) or compensated cirrhosis (Metavir F4)

Rating: Class I, Level A

Organ transplant

Rating: Class I, Level B

Type 2 or 3 essential mixed cryoglobulinemia with end-organ manifestations (eg, vasculitis)

Rating: Class I, Level B

Proteinuria, nephrotic syndrome, or membranoproliferative glomerulonephritis

Rating: Class IIa, Level B

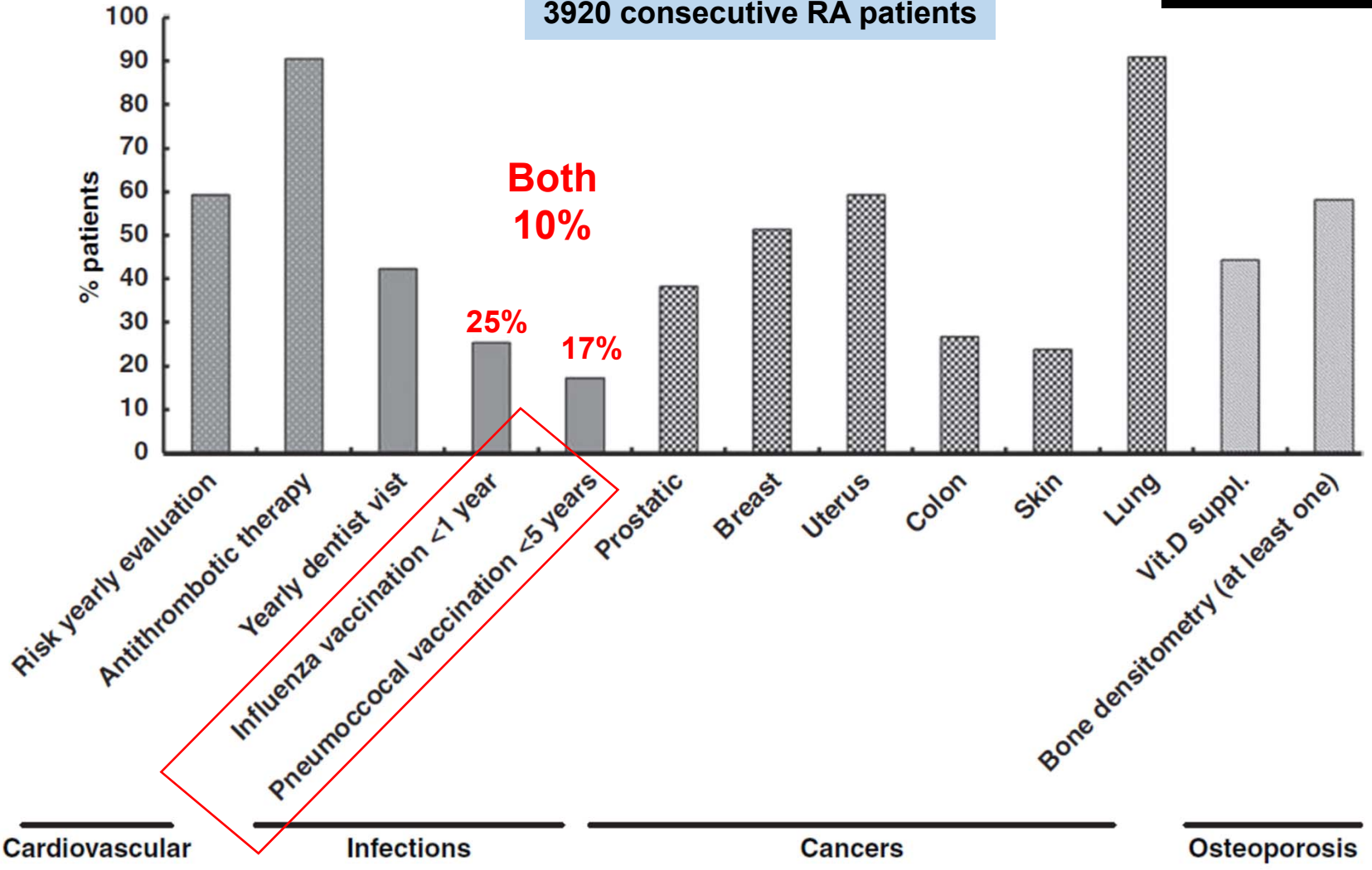
Available at: *http://www.hcvguidelines.org/*

- **Therapeutic regimens based on:**
  - ***viral genotype (1,2,3,4)***
  - ***cirrhosis or not***
  - ***antiviral treatment naïve or experienced***
- **Limited data with the new generation of DAAs in HCV-associated CV** ***Vassilopoulos D/Calabrese LH Curr Rheum Rep 2015 (in press)***

Vaccinations in RA patients: Are we doing them?

COMORA Study
17 international centers
3920 consecutive RA patients

Age = 56 yrs
♂ = 20%
Dis. duration = 10 yrs



Dougados M, *et al*. *Ann Rheum Dis* 2014;**73**:62–68.

Vaccinations in AS patients: Are we doing them?

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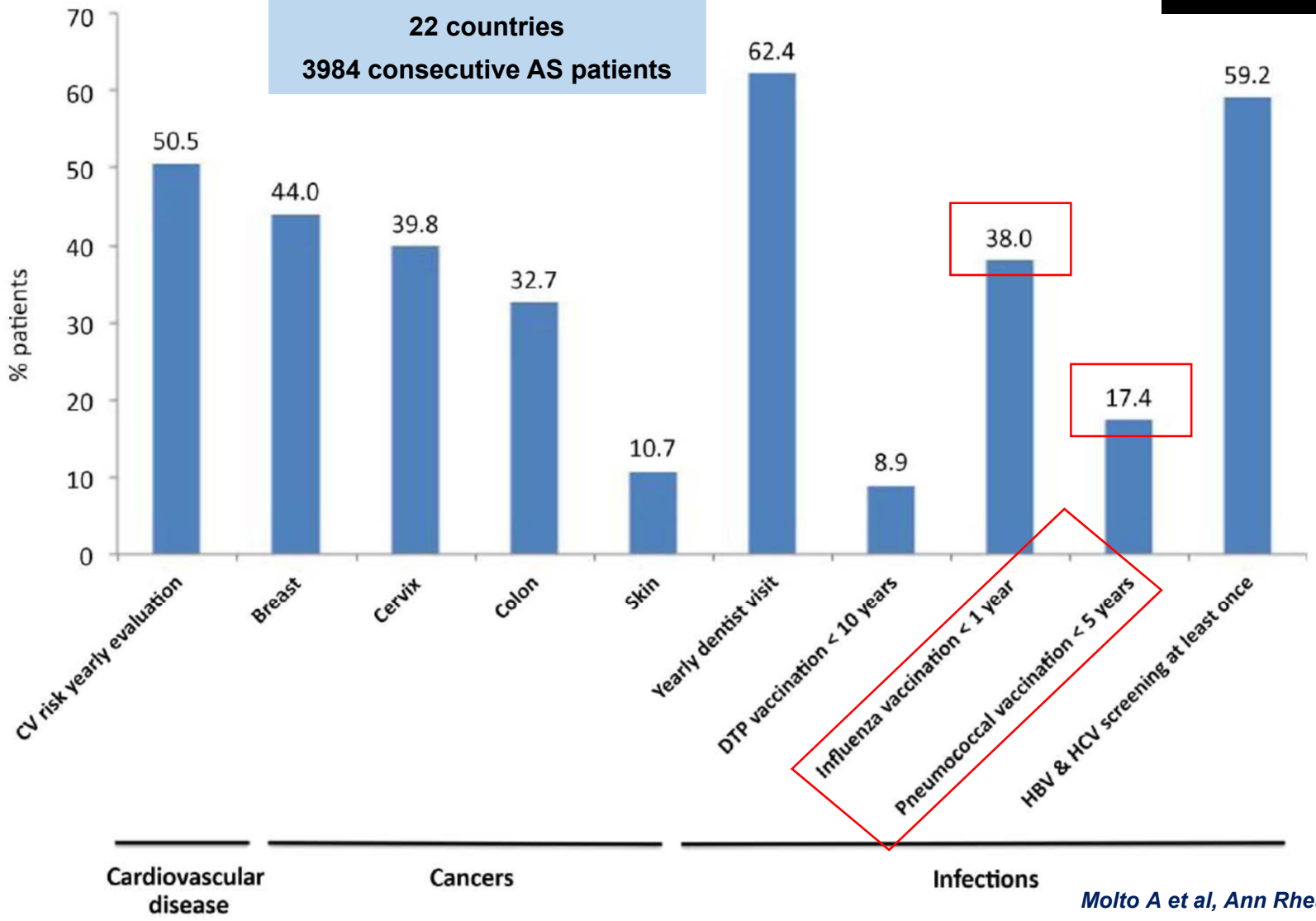


Molto A et al, Ann Rheum Dis 2015

Vaccinations in adult immunocompromised patients

Recommended Adult Immunization Schedule—United States • 2015

VACCINE ▼ INDICATION ▶	Pregnancy	Immuno-compromising conditions (excluding human immunodeficiency virus [HIV])[4,6,7,8,13]	HIV infection CD4+ T lymphocyte count[4,6,7,8,13] <200 cells/µL	HIV infection CD4+ T lymphocyte count[4,6,7,8,13] ≥200 cells/µL	Men who have sex with men (MSM)	Kidney failure, end-stage renal disease, receipt of hemodialysis	Heart disease, chronic lung disease, chronic alcoholism	Asplenia (including elective splenectomy and persistent complement component deficiencies)[8,12]	Chronic liver disease	Diabetes	Health care personnel
Influenza[2,*]		1 dose IIV annually			1 dose IIV or LAIV annually	1 dose IIV annually					1 dose IIV or LAIV annually
Tetanus, diphtheria, pertussis (Td/Tdap)[3,*]	1 dose Tdap each pregnancy	Substitute 1-time dose of Tdap for Td booster; then boost with Td every 10 yrs									
Varicella[4,*]	Contraindicated			2 doses							
Human papillomavirus (HPV) Female[5,*]	3 doses through age 26 yrs				3 doses through age 26 yrs						
Human papillomavirus (HPV) Male[5,*]	3 doses through age 26 yrs				3 doses through age 21 yrs						
Zoster[6]	Contraindicated			1 dose							
Measles, mumps, rubella (MMR)[7,*]	Contraindicated			1 or 2 doses							
Pneumococcal 13-valent conjugate (PCV13)[8,*]	1 dose										
Pneumococcal polysaccharide (PPSV23)[8]	1 or 2 doses										
Meningococcal[9,*]	1 or more doses										
Hepatitis A[10,*]	2 doses										
Hepatitis B[11,*]	3 doses										
Haemophilus influenzae type b (Hib)[12,*]	post-HSCT recipients only	1 or 3 doses									

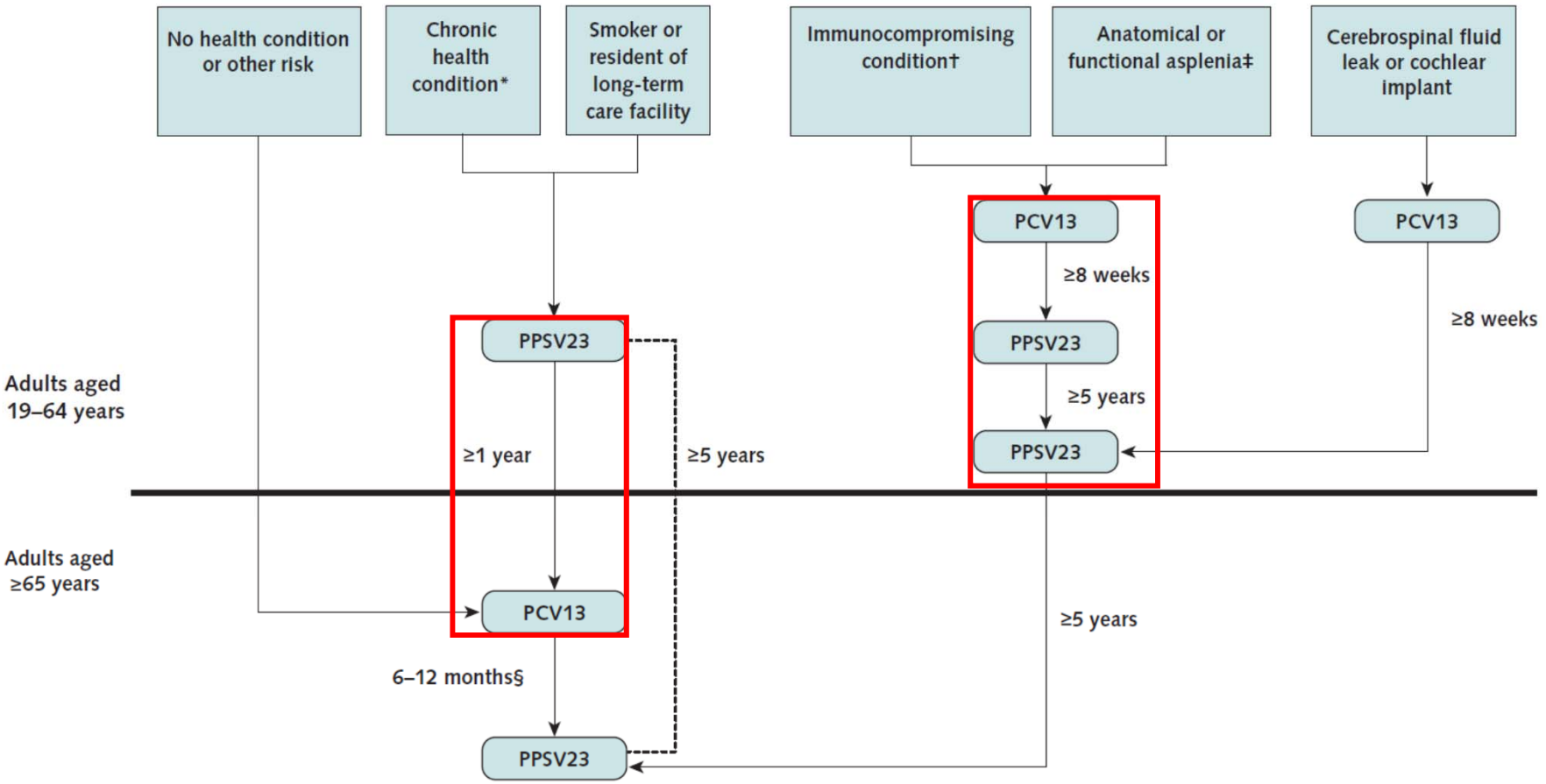
For all persons in this category who meet the age requirements and who lack documentation of vaccination or have no evidence of previous infection; zoster vaccine recommended regardless of prior episode of zoster

Recommended if some other risk factor is present (e.g., on the basis of medical, occupational, lifestyle, or other indications)

No recommendation

Kim DK et al, Ann Intern Med 2015

Pneumococcal vaccine 2015



Kim DK et al, Ann Intern Med 2015

Human papilloma virus (HPV) vaccination in young ♀ with JIA

EXTENDED REPORT

Immunogenicity and safety of the bivalent HPV vaccine in female patients with juvenile idiopathic arthritis: a prospective controlled observational cohort study

Marloes W Heijstek,[1] Mirte Scherpenisse,[2,3] Noortje Groot,[1] Carline Tacke,[1] Rutger M Schepp,[2] Anne-Marie Buisman,[2] Guy A M Berbers,[2] Fiona R M van der Klis,[2] Nico M Wulffraat[1]

Heijstek MW, *et al*. *Ann Rheum Dis* 2014;**73**:1500–1507

Prospective, observational controlled cohort study

♀

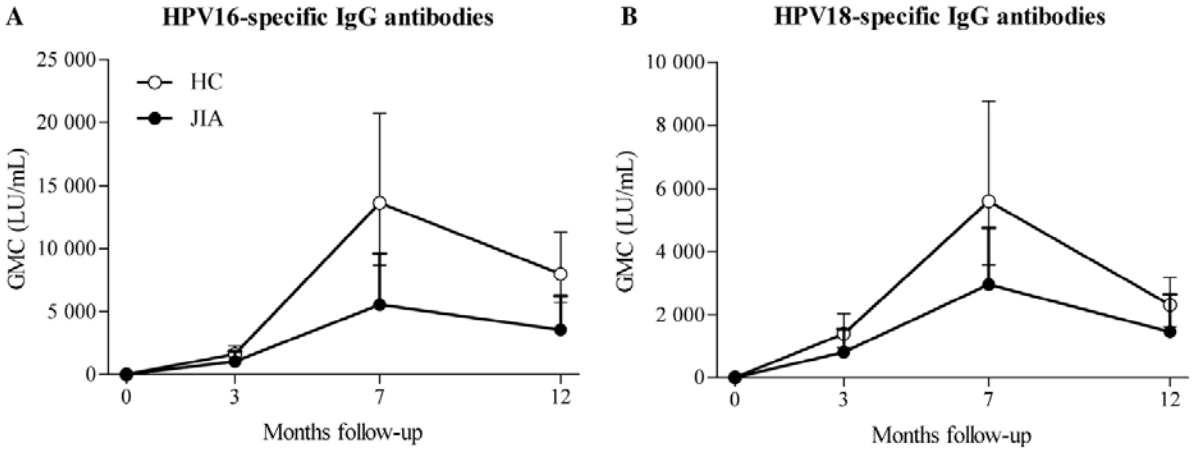
n=68 pts with JIA 12-18 yrs
n=55 healthy controls

Bivalent HP Vaccine (GSK)

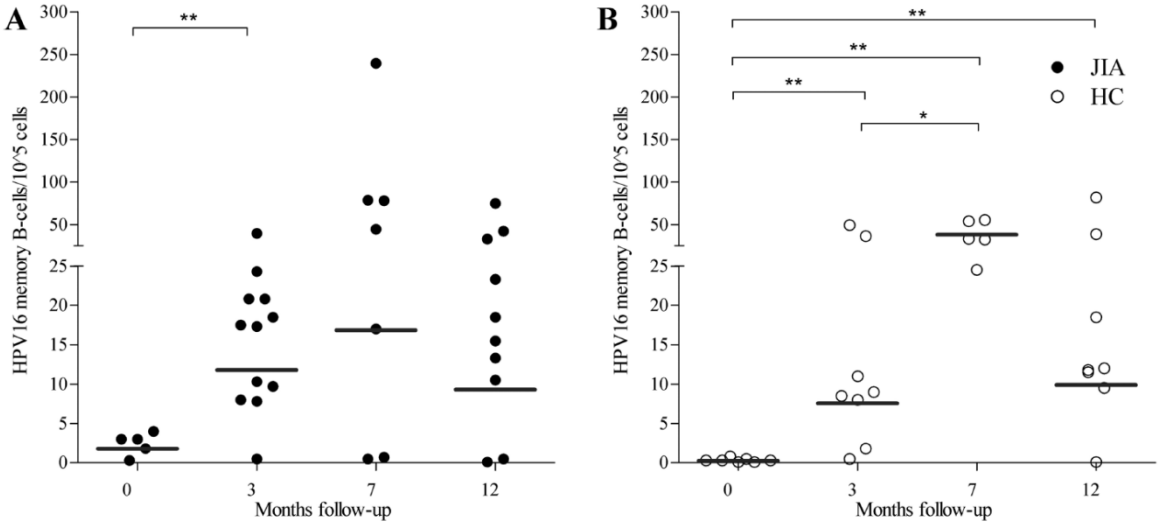
0-1-6 months

The Netherlands

100% Seropositivity



Memory specific B cells



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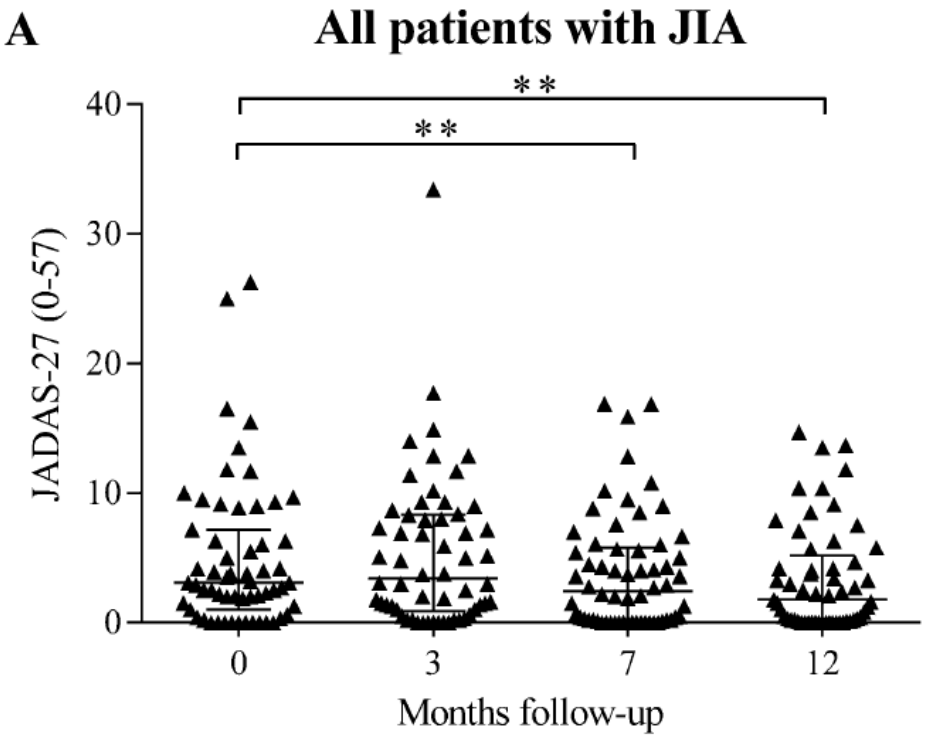
Heijstek MW, *et al*. *Ann Rheum Dis* 2014;**73**:1500–1507

No effect of Rx (MTX/anti-TNF) on immunogenicity

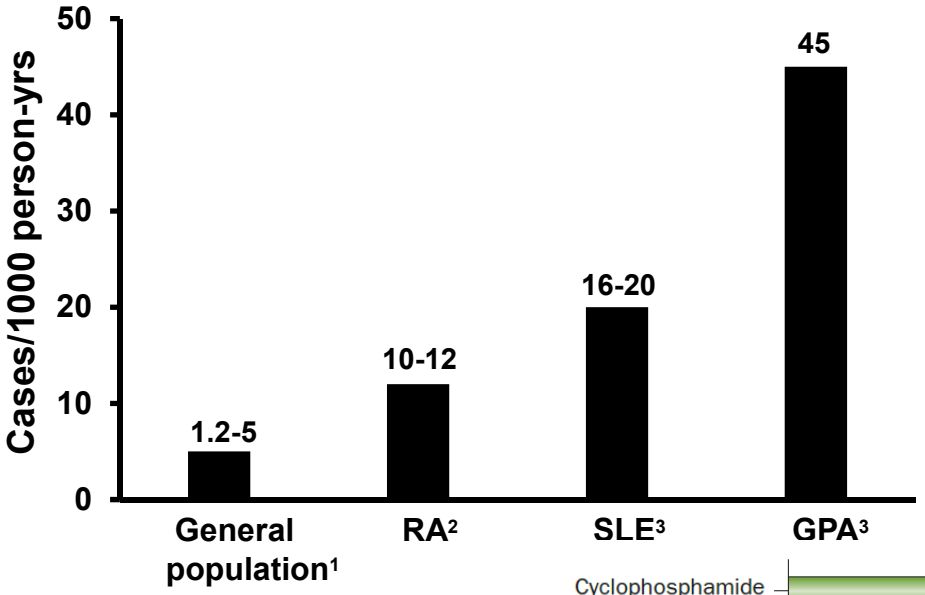
Effect on disease activity



- **HPV is safe and immunogenic in young ♀ (12-18) pts with JIA, regardless of underlying immunosuppressive therapy**

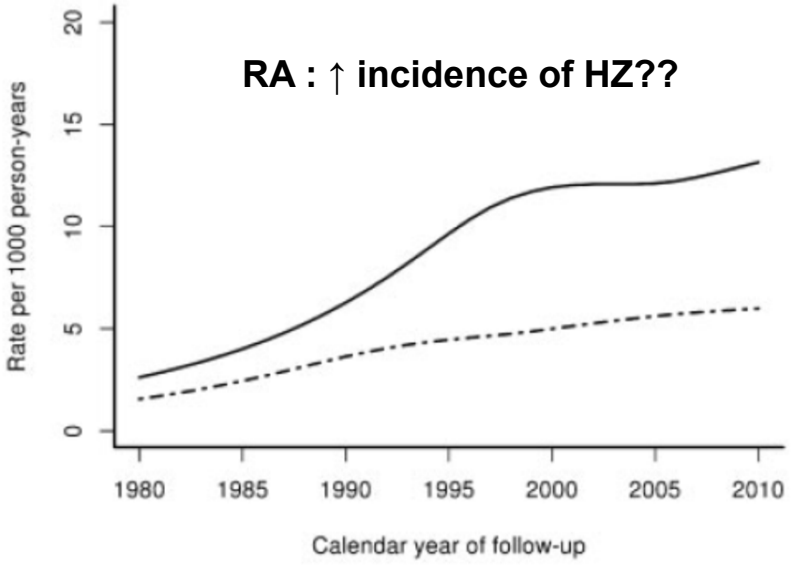
- **No effect on disease activity**

Herpes zoster in rheumatic patients



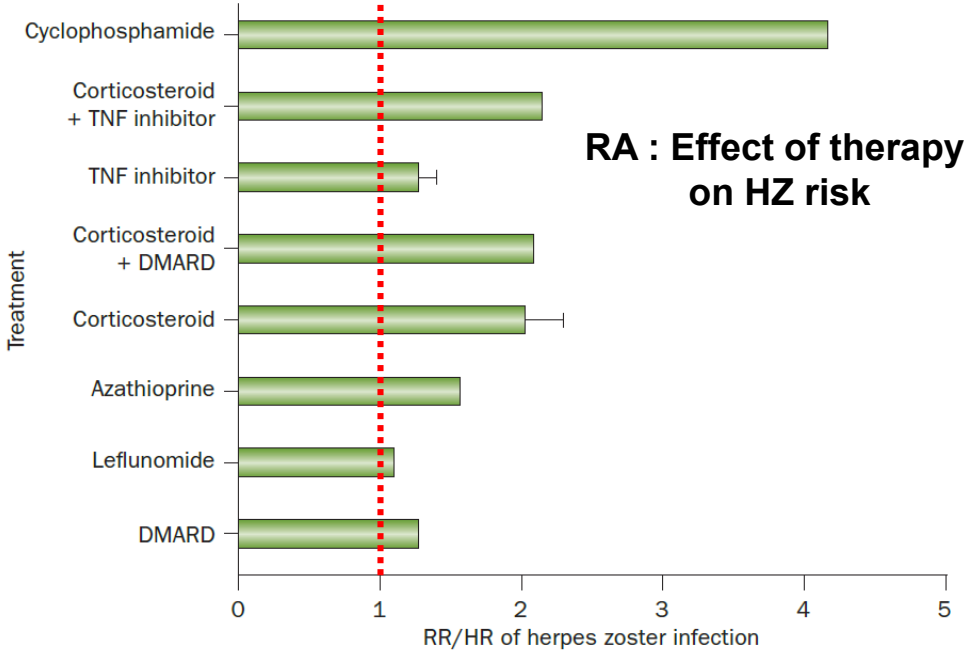
[1]Cohen JI, NEJM 2013
[2]Vetil BM, Arthritis Care & Res 2013
[3]Wung PK, Am J Med 2005

RA : ↑ incidence of HZ??



Vetil BM, Arthritis Care & Res 2013

RA : Effect of therapy on HZ risk



Westra, J. *et al. Nat. Rev. Rheumatol*. advance online publication 9 December 2014;

Herpes Zoster Vaccine

Herpes Zoster Vaccine
(Live Attenuated Vaccine)

Single SC dose

Approved for the general population
(regardless of history of herpes zoster):

≥ 50 yrs (Sweden)
≥ 60 yrs (Greece/USA/Australia/Canada)
≥ 70 yrs (UK)

↓ risk for:

Herpes Zoster (HZ)	**~ 50%**
Post-herpetic neuralgia (PHN)	**~ 65%**

Gagliardi AM, Cochrane Database Syst Rev 2012
Cohen JI, NEJM 2013

Contra-indications

- Hematologic cancers not in remission
- Recent chemotherapy (< 3mo)
- HIV (CD4 < 200/μL)
- **High dose immunosuppressive therapy**
  - ✓ **Prednisolone ≥ 20 mg x > 2 weeks**
  - ✓ **Anti-TNFs**

Cohen JI, NEJM 2013

Herpes zoster Vaccine – DMARDs

ACR 2012

Table 5. 2012 American College of Rheumatology recommendations update regarding the use of vaccines in patients with RA starting or currently receiving DMARDs or biologic agents*

	Killed vaccines			Recombinant vaccine	Live attenuated vaccine
	Pneumococcal†	Influenza (intramuscular)	Hepatitis B‡	Human papillomavirus	Herpes zoster
Before initiating therapy					
DMARD monotherapy	✓	✓	✓	✓	✓
Combination DMARDs§	✓	✓	✓	✓	✓
Anti-TNF biologics¶	✓	✓	✓	✓	✓
Non-TNF biologics#	✓	✓	✓	✓	✓
While already taking therapy					
DMARD monotherapy	✓	✓	✓	✓	✓
Combination DMARDs	✓	✓	✓	✓	✓
Anti-TNF biologics¶	✓	✓	✓	✓	Not recommended**
Non-TNF biologics#	✓	✓	✓	✓	Not recommended**

Singh JA, Arthritis Care & Res 2012

Herpes zoster Vaccine – DMARDs (biologics or not)

Association Between Vaccination for Herpes Zoster and Risk of Herpes Zoster Infection Among Older Patients With Selected Immune-Mediated Diseases

Jie Zhang, PhD
Fenglong Xie, MS
Elizabeth Delzell, ScD
Lang Chen, PhD
Kevin L. Winthrop, MD, MPH
James D. Lewis, MD, MSCE
Kenneth G. Saag, MD, MSc
John W. Baddley, MD, MSPH
Jeffrey R. Curtis, MD, MS, MPH

JAMA, July 4, 2012—Vol 308, No. 1 43

- Retrospective data on ~ 465,000 pts with RA, PsO, PsA, IBD, AS
- < 5% (~19,000) received the HZ vaccine
- Similar efficacy to healthy individuals
  - ↓ HZ (Adjusted HR: 0.61)
  - ↓ PHN by 80%
- n=633 on biologics (87%: anti-TNF):

No cases of varicella or HZ

AMERICAN COLLEGE OF RHEUMATOLOGY
EDUCATION • TREATMENT • RESEARCH

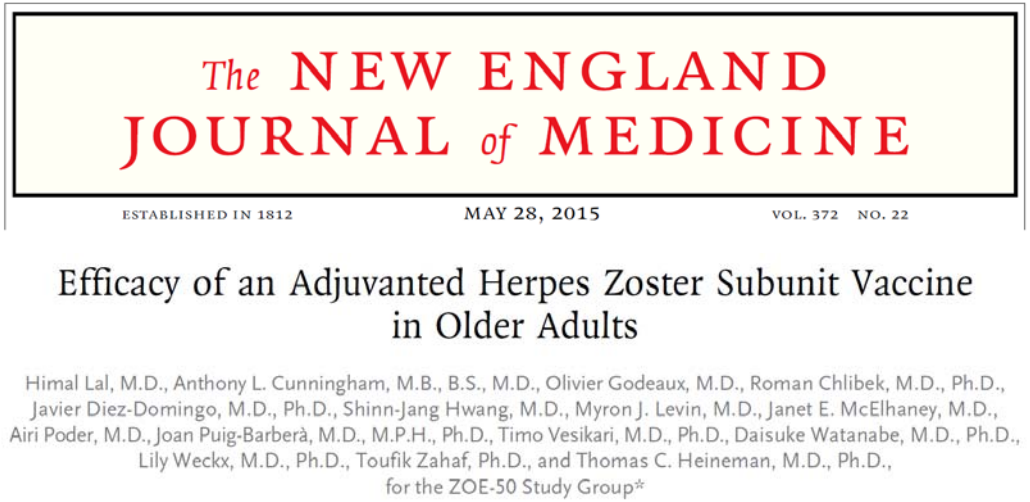
Update on Herpes Zoster (Shingles) Vaccine for Autoimmune Disease Patients

September 21, 2012

- The vaccine is currently considered inadvisable for patients treated with biologic therapies. For these patients, it may be reasonable to hold the biologic for a period of time, vaccinate, and resume the biologic approximately 30 days later. However, patients may be reluctant to do this given concerns for disease flare during the time that the biologic is being held.

http://www.rheumatology.org/Publications/Hotline/Update_on_Herpes_Zoster_%28Shingles%29_Vaccine_for_Autoimmune_Disease_Patients/

Herpes zoster Vaccine: What is coming and what to remember?



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MAY 28, 2015 VOL. 372 NO. 22

Efficacy of an Adjuvanted Herpes Zoster Subunit Vaccine in Older Adults

Himal Lal, M.D., Anthony L. Cunningham, M.B., B.S., M.D., Olivier Godeaux, M.D., Roman Chlibek, M.D., Ph.D., Javier Diez-Domingo, M.D., Ph.D., Shinn-Jang Hwang, M.D., Myron J. Levin, M.D., Janet E. McElhaney, M.D., Airi Poder, M.D., Joan Puig-Barberà, M.D., M.P.H., Ph.D., Timo Vesikari, M.D., Ph.D., Daisuke Watanabe, M.D., Ph.D., Lily Weckx, M.D., Ph.D., Toufik Zahaf, Ph.D., and Thomas C. Heineman, M.D., Ph.D., for the ZOE-50 Study Group*

Recombinant subunit vaccine

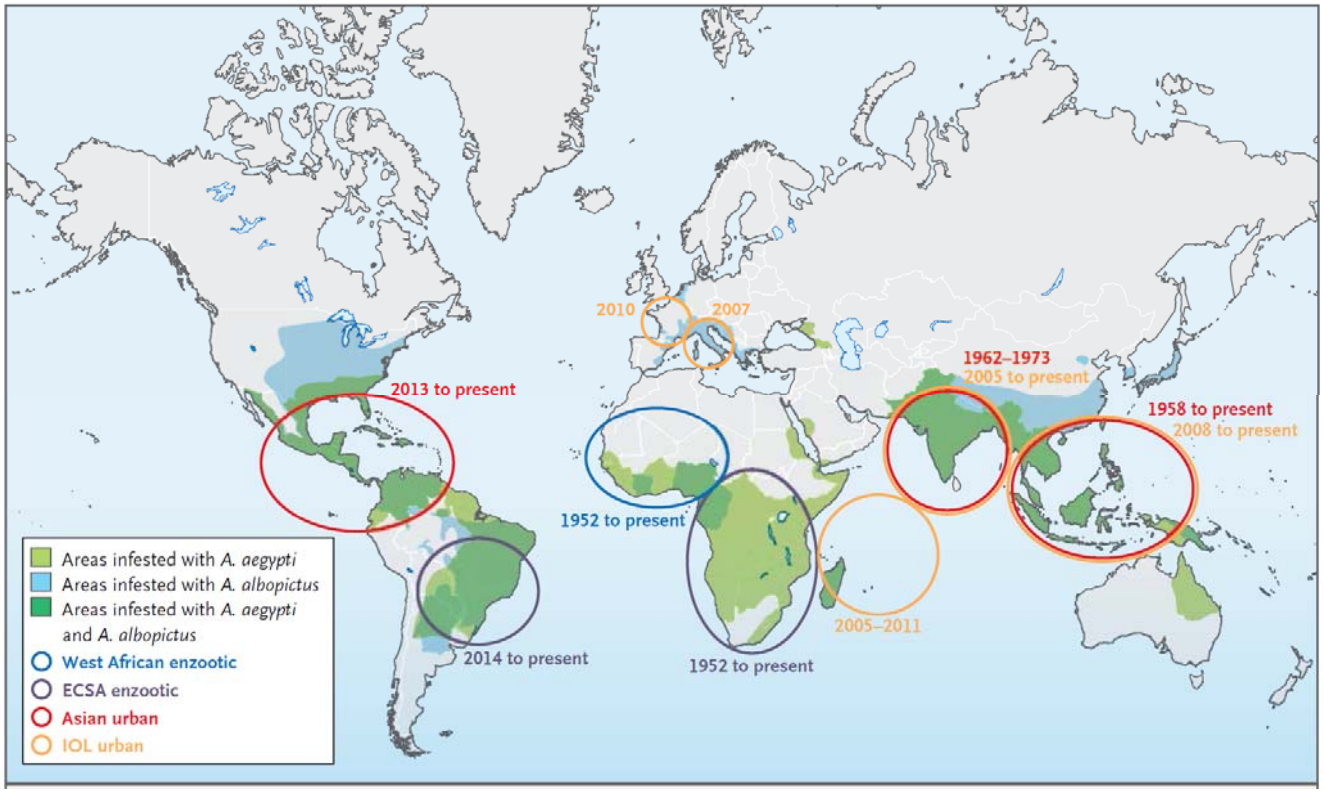
- **97% efficacious**
- **For all age groups (≥ 50 yrs)**
- **No significant side-effects**
- **No data on immunosuppressed pts yet**

- **HZV is equally efficacious in immunocompromised patients compared to the general population**

- **It can be administered in patients on low-dose steroids (<20 mg/d) and csDMARDs and before starting bDMARDs**

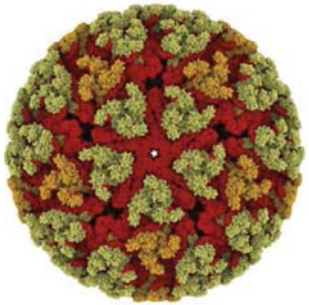
- **More data for its safety are needed for patients on chronic therapy with bDMARDs**

Chikungunya virus (CHIKV)



Weaver SC et al, NEJM 2015

- **Mosquito –borne alpha virus**
- **Most common in Africa**
- **Recent outbreaks in:**
  - **Indian Ocean islands/India**
    - **→ Italy/France *(2007-2010)***
  - **Caribbean/Central America *(2013)***
- **Cause of arthritis (RA-like)**



Sinclair Stammers/Science Photo Library

CHIKV-related arthritis

Chikungunya Viral Arthritis in the United States

A Mimic of Seronegative Rheumatoid Arthritis

Jonathan J. Miner,[1] Han Xian Aw Yeang,[1] Julie M. Fox,[1] Samantha Taffner,[1] Olga N. Malkova,[1] Stephen T. Oh,[1] Alfred H. J. Kim,[1] Michael S. Diamond,[1] Deborah J. Lenschow,[1] and Wayne M. Yokoyama[2]

ARTHRITIS & RHEUMATOLOGY
Vol. 67, No. 5, May 2015, pp 1214–1220
DOI 10.1002/art.39027

n=10 patients
Travellers to Haiti (06/2104)

8 with acute arthritis
(2010 ACR/EULAR RA criteria: +)

+

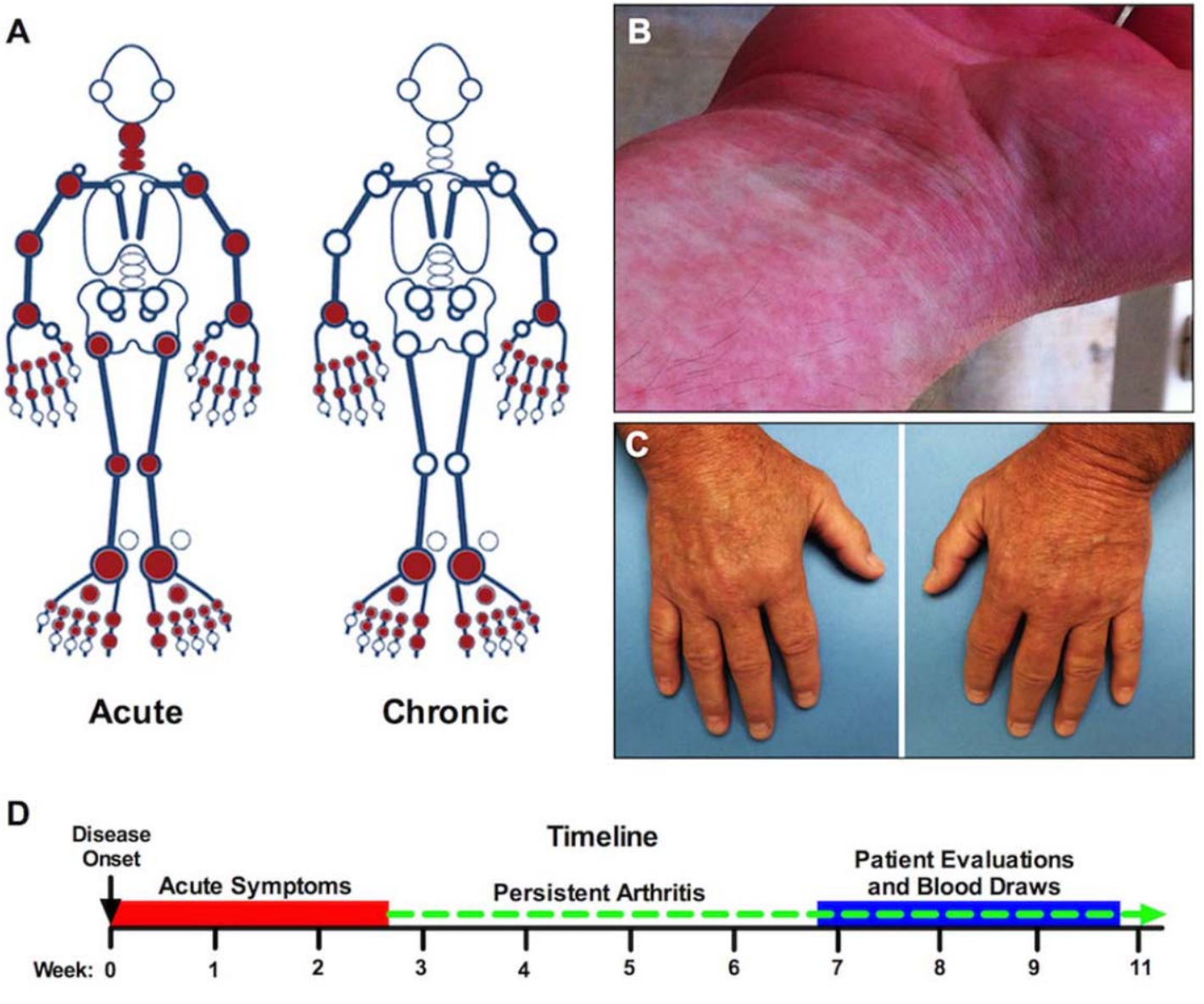
Fever
Rash
Arthritis

+

Normal ESR (100%)
--//-- CRP (80%)

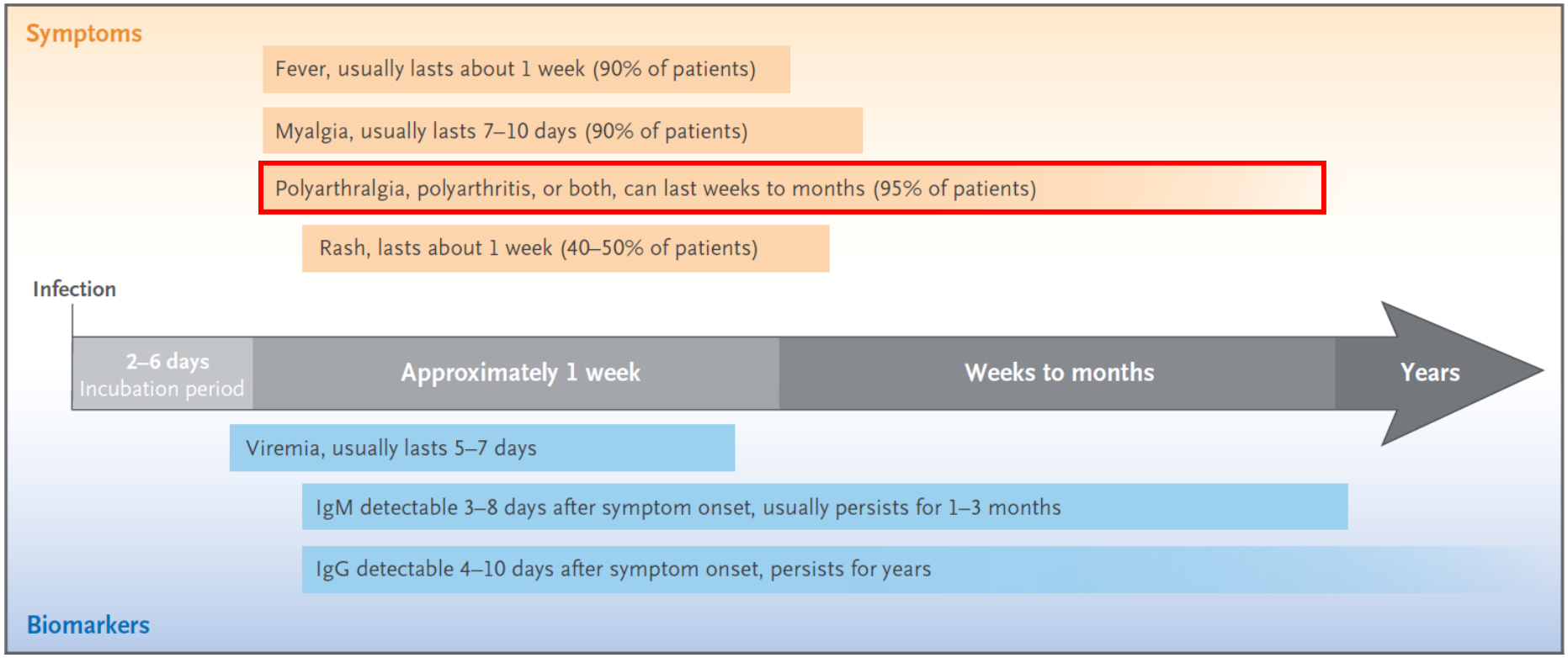
RF/anti-CCP: (-)/(-)
ANA: 3/10 (30%) (+)

CHIKV-related arthritis



Miner JJ et al, Arthritis & Rheumatol 2015

CHIKV-related arthritis: When to think about it?



Weaver SC et al, NEJM 2015

Think about it
in patients with an acute seronegative polyarthritis
and
Recent travel to endemic areas (Caribbean, Africa, India…)
accompanied by:
Fever, rash, myalgias

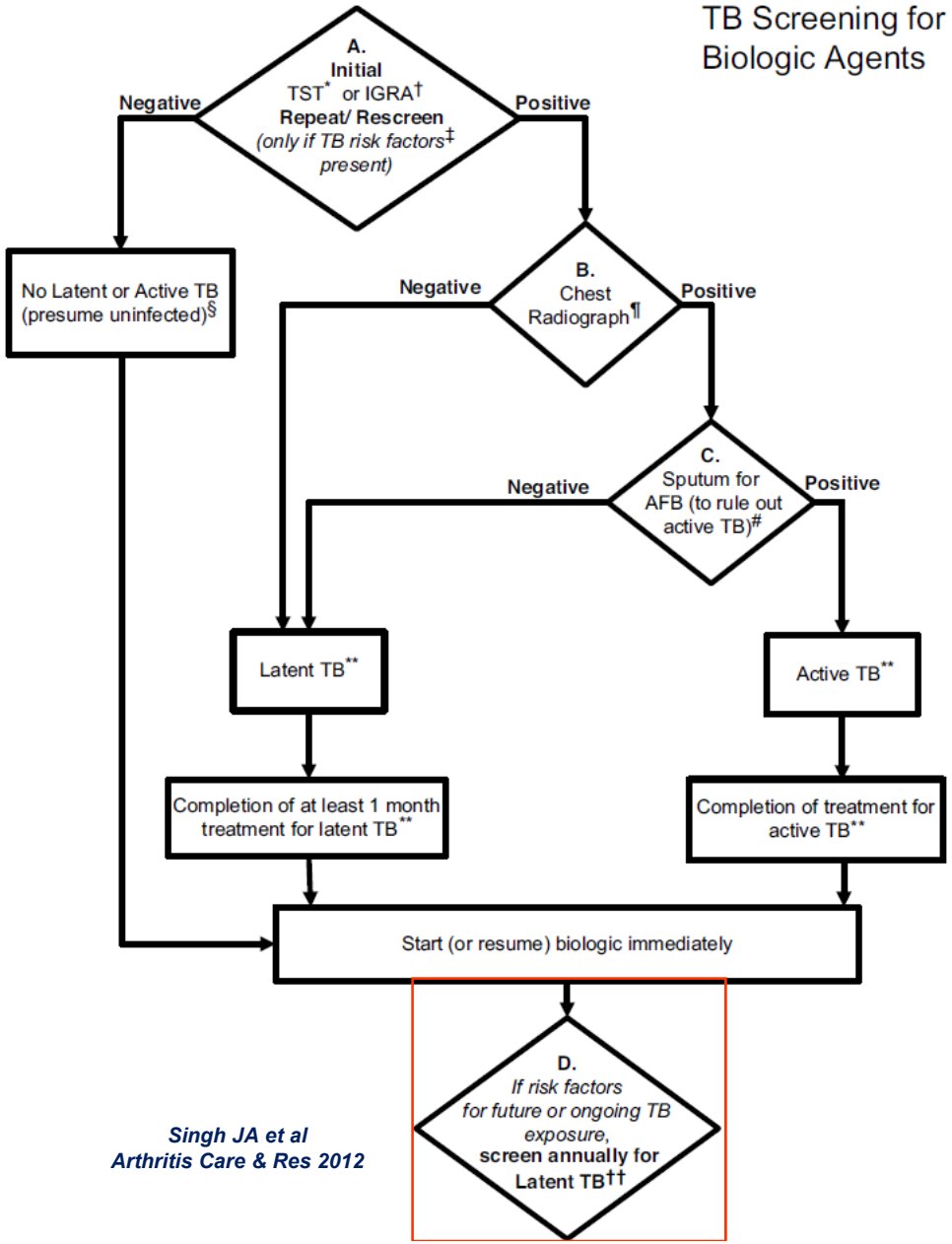
Tuberculosis

Do we need to re-screen

LTBI negative patients

on chronic biologic therapy?

Re-screening for TB during biologic treatment



Singh JA et al
Arthritis Care & Res 2012

Updated consensus statement on biological agents for the treatment of rheumatic diseases, 2012

Daniel E Furst,[1] Edward Clark Keystone,[2] Alexander K So, Jürgen Braun,[3] Ferry C Breedveld,[4] Gerd R Burmester,[5] Fabrizio De Benedetti,[6] Thomas Dörner,[7] Paul Emery,[8] Roy Fleischmann,[9] Allan Gibofsky,[10] J R Kalden,[11] Arthur Kavanaugh,[12] Bruce Kirkham,[13] Philip Mease,[14] A Rubbert-Roth,[15] Joachim Sieper,[16] Nora G Singer,[17] Josef S Smolen,[18,19] Piet L C M Van Riel,[20] Michael H Weisman,[21] Kevin L Winthrop[22]

In areas of high TB prevalence (ie, high-risk populations or in the event of potential TB exposure), repeat screening should be considered (category C evidence[477 492 493]).

Ann Rheum Dis 2013;**72**:ii2–ii34.

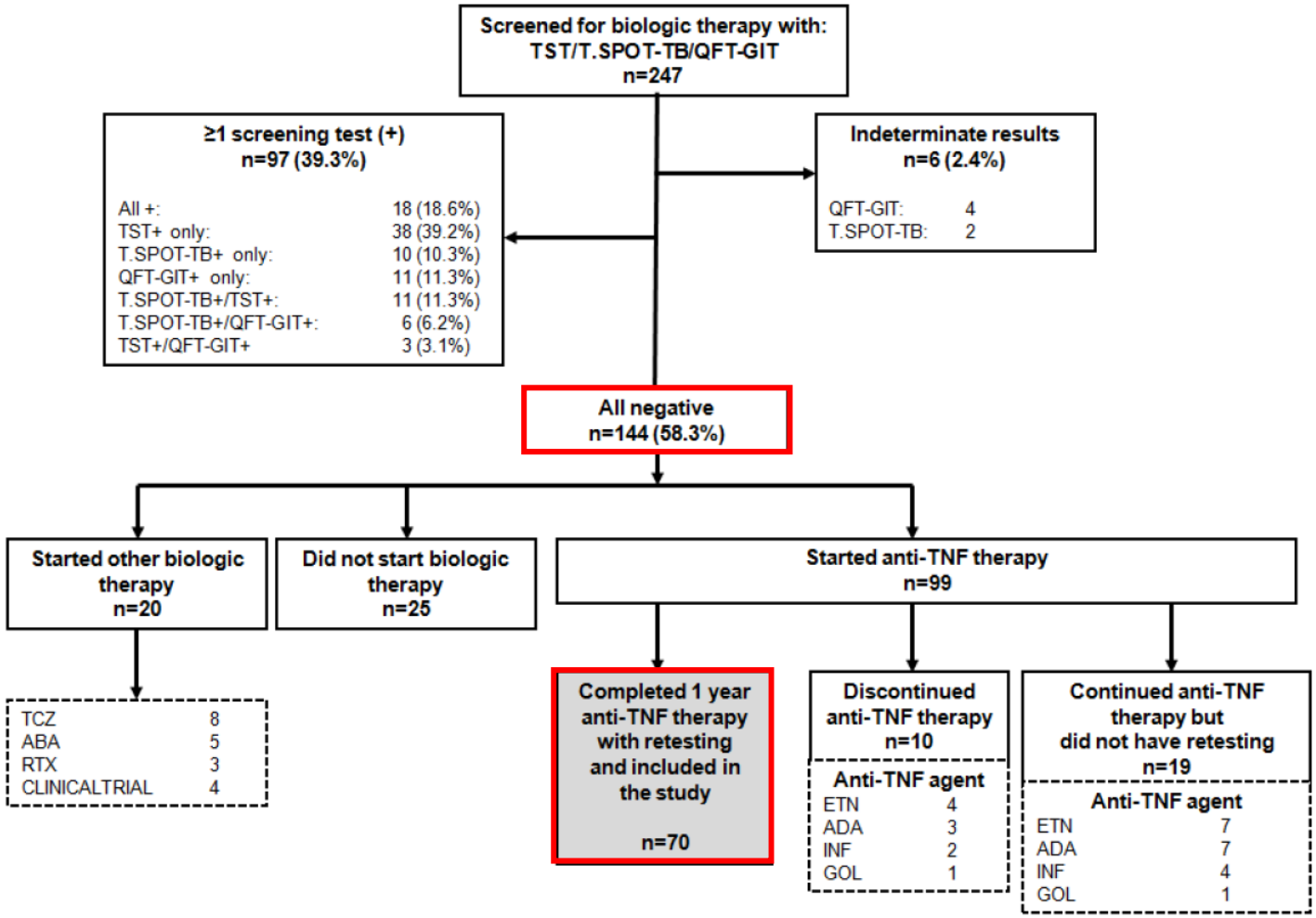
Re-screening for TB during anti-TNF treatment

EXTENDED REPORT

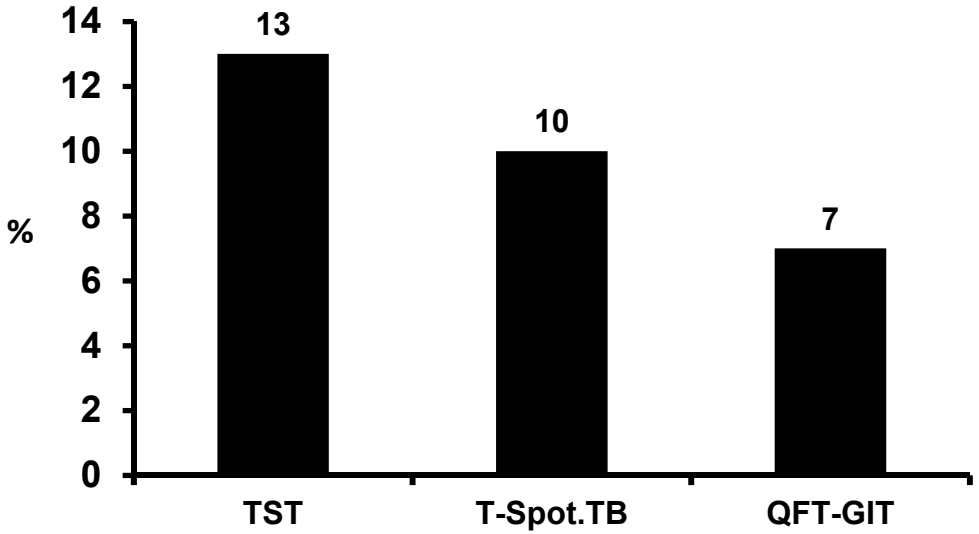
Frequent conversion of tuberculosis screening tests during anti-tumour necrosis factor therapy in patients with rheumatic diseases

Chrisoula Hatzara, Emilia Hadziyannis, Anna Kandili, Christos Koutsianas, Anastasia Makris, Georgios Georgiopoulos, Dimitrios Vassilopoulos

Ann Rheum Dis 2014;**0**:1–6. doi:10.1136/annrheumdis-2014-205376



Re-screening for TB during anti-TNF treatment



n=20 (29%)

Conversion of ≥1 screening assay

- **n=1, with 2 positive assays (TST/QFT.GIT)**
  Born in a high-prevalence area
- **n=1, T-Spot.TB (+): Definite TB exposure**
- **No patient developed TB (40% on INH)**

	Multivariate analysis†	
Characteristic	**OR (95% CI)**	**p Value**
Age >50 years	1.18 (0.296 to 4.73)	0.812
Sex	0.843 (0.179 to 3.97)	0.829
RA (vs non-RA)	1.45 (0.284 to 7.45)	0.653
Possible previous TB exposure‡	**7.24 (1.09 to 48)**	**0.04**
Previous BCG vaccination	0.556 (0.142 to 2.18)	0.399
Steroids or DMARDs	0.265 (0.052 to 1.35)	0.109
Adalimumab/other anti-TNFs		
Infliximab	**0.031 (0.002 to 0.414)**	**0.009**
Etanercept		

Ann Rheum Dis 2014;**0**:1–6. doi:10.1136/annrheumdis-2014-205376

Re-screening for TB in Healthcare Workers (HCWs)

Interferon-γ Release Assays and Tuberculin Skin Testing for Diagnosis of Latent Tuberculosis Infection in Healthcare Workers in the United States

Susan E. Dorman[1], Robert Belknap[2,3], Edward A. Graviss[4], Randall Reves[2,3], Neil Schluger[5], Paul Weinfurter[6], Yaping Wang[1], Wendy Cronin[7], Yael Hirsch-Moverman[5], Larry D. Teeter[4], Matthew Parker[2,3], Denise O. Garrett[8], and Charles L. Daley[9,10]; for the Tuberculosis Epidemiologic Studies Consortium

Am J Respir Crit Care Med Vol 189, Iss 1, pp 77–87, Jan 1, 2014

n=2,418 HCWs

Conversion rate: **T-Spot.TB: 8.3%** **QFT-GIT: 6.1%**

→ **Retesting: (6 months later)** **T-Spot.TB/QFT-GIT 77% Negative**

- **TB test conversions can occur during anti-TNF therapy (~10%)**
- **Unclear at the moment if they represent "true conversions"**
- **More data are needed in order to recommend universal re-screening in the absence of definite exposure, especially in low-prevalence countries**

Serious infections in RA

After 15 years of biologics and a large number of RCTs

in RA,

what is the risk of serious infections

compared to traditional DMARDs?

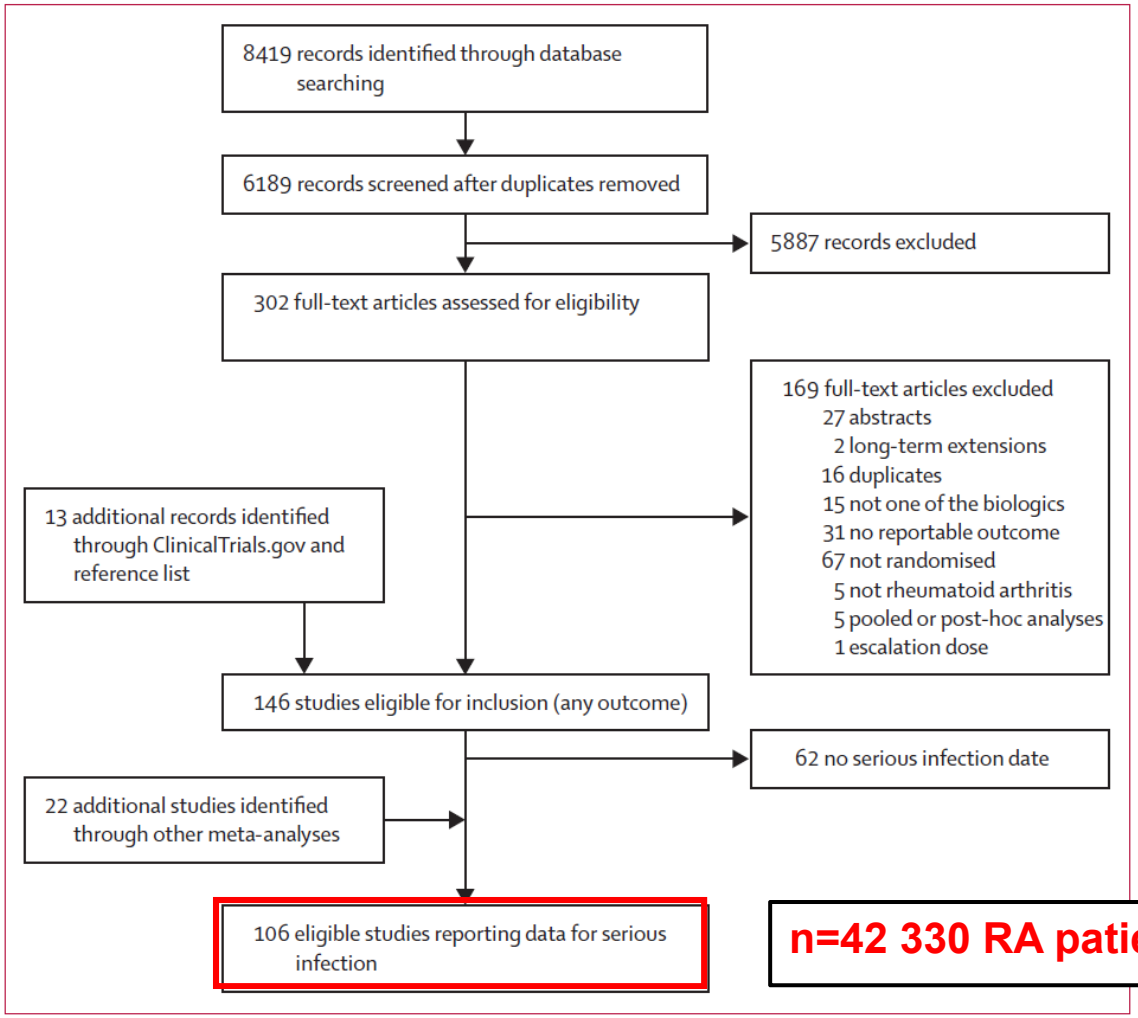
Risk for serious infections in RA patients on biologics

Risk of serious infection in biological treatment of patients with rheumatoid arthritis: a systematic review and meta-analysis

Jasvinder A Singh, Chris Cameron*, Shahrzad Noorbaloochi, Tyler Cullis, Matthew Tucker, Robin Christensen, Elizabeth Tanjong Ghogomu, Doug Coyle, Tammy Clifford, Peter Tugwell, George A Wells*

www.thelancet.com **Published online May 12, 2015**

RCTs

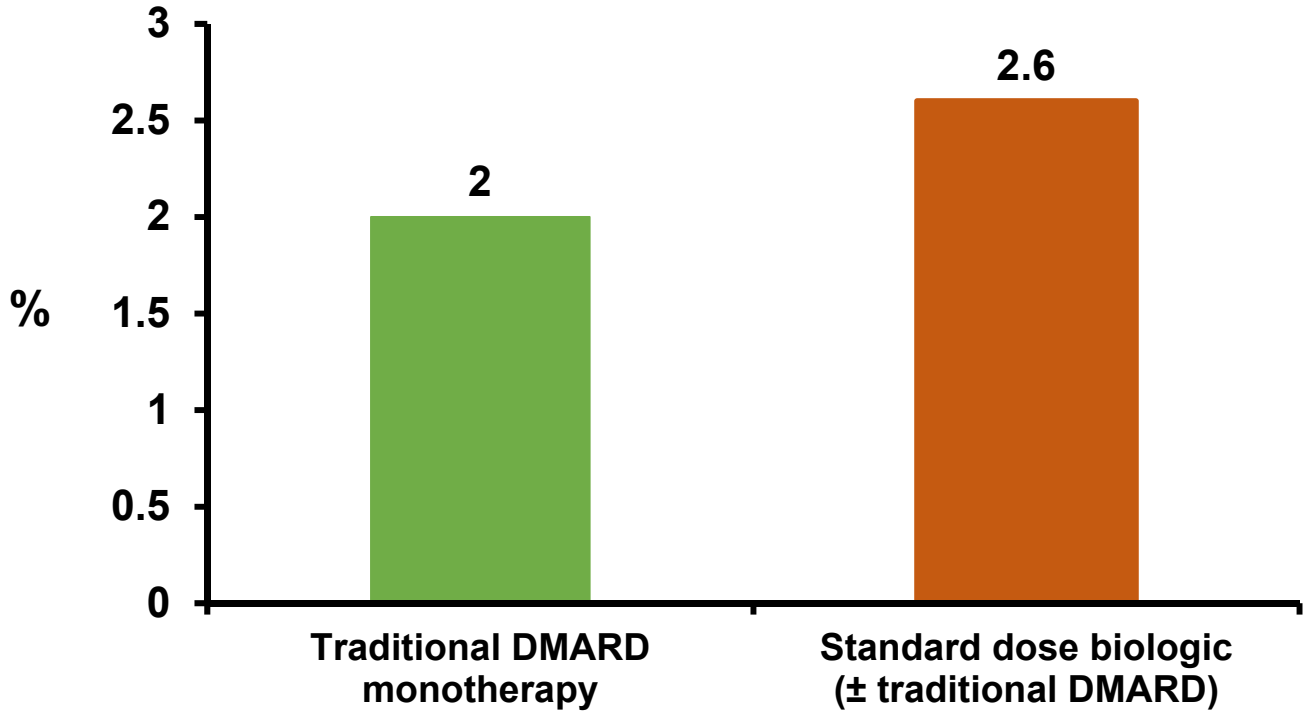


n=42 330 RA patients

Risk for serious infections in RA patients on biologics

			OR (95% Credible Intervals)
Standard dose biologic DMARD (± traditional DMARD)	vs.	Traditional DMARD monotherapy	1.31 (1.09-1.58)

Absolute annual risk for serious infection (median)



Singh JA et al, Lancet 2015

Serious infections in SLE

CONNECTIVE TISSUE DISEASES

The burden of serious infections in SLE

Jessica Widdifield and Sasha Bernatsky

NATURE REVIEWS | RHEUMATOLOGY
doi:10.1038/nrrheum.2015.55
Published online 21 April 2015

- **20-30% of deaths in SLE are due to infections**

- **What is the rate and risk factors for serious infections in SLE patients?**

- **Are these increasing over the last decades?**

SLE and serious infections

Serious Infections Among Adult Medicaid Beneficiaries With Systemic Lupus Erythematosus and Lupus Nephritis

Candace H. Feldman,[1] Linda T. Hiraki,[2] Wolfgang C. Winkelmayer,[3] Francisco M. Marty,[4] Jessica M. Franklin,[4] Seoyoung C. Kim,[4] and Karen H. Costenbader[4]

ARTHRITIS & RHEUMATOLOGY
Vol. 67, No. 6, June 2015, pp 1577–1585

	Serious infections/ 100 pt-yrs*	Mortality rate after infection/ 100 pt-yrs	In hospital or 30 d after mortality rate/ 100 pt-yrs
SLE	10.8	4.7	2.1
Lupus nephritis	23.9	7.9	3.9

RA = 2.2-5/100 pt-yrs

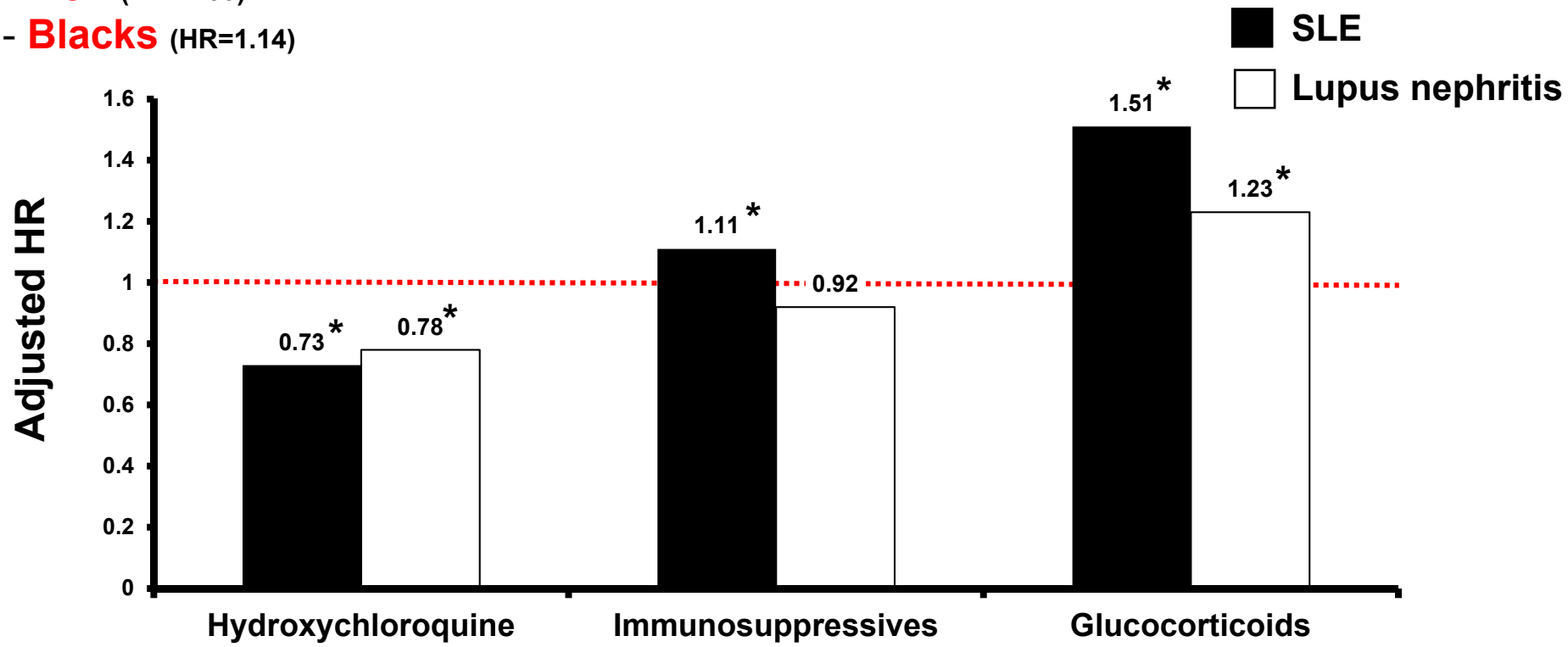
~ 45% of deaths from serious infections during hospitalization or shortly after (1 mo)

** Bacterial (96%), viral (2.7%), fungal (0.7%), mycobacterial (0.6%)*

Medications and risk for hospitalized infections in SLE patients

Risk for the 1st serious hospitalized infections

- **Men** (HR=1.33)
- **Blacks** (HR=1.14)

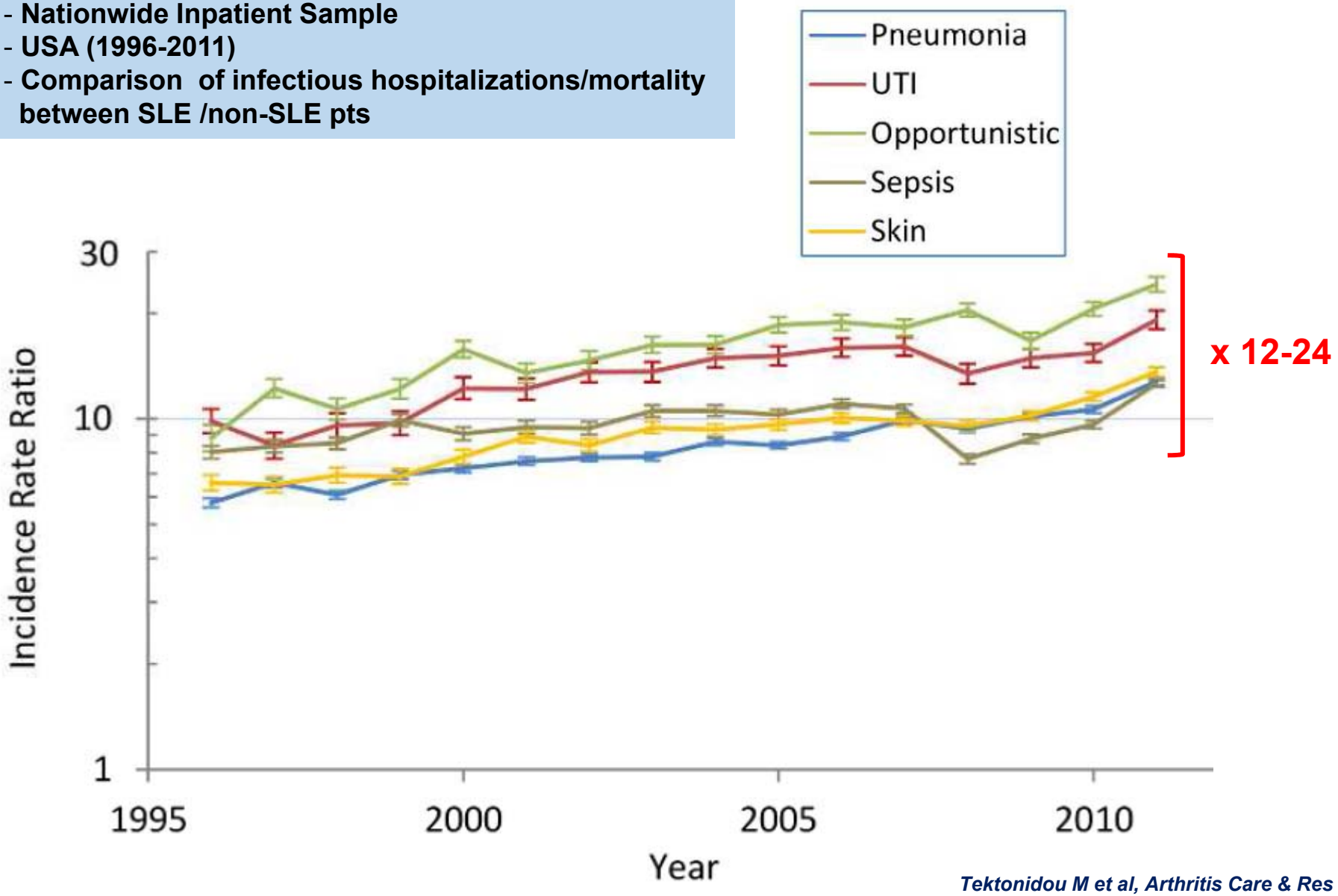


* p<0.05

Feldman CH et al, Arthritis & Rheumatol 2015

Risk for infectious hospitalizations in SLE patients

- **Nationwide Inpatient Sample**
- **USA (1996-2011)**
- **Comparison of infectious hospitalizations/mortality between SLE /non-SLE pts**

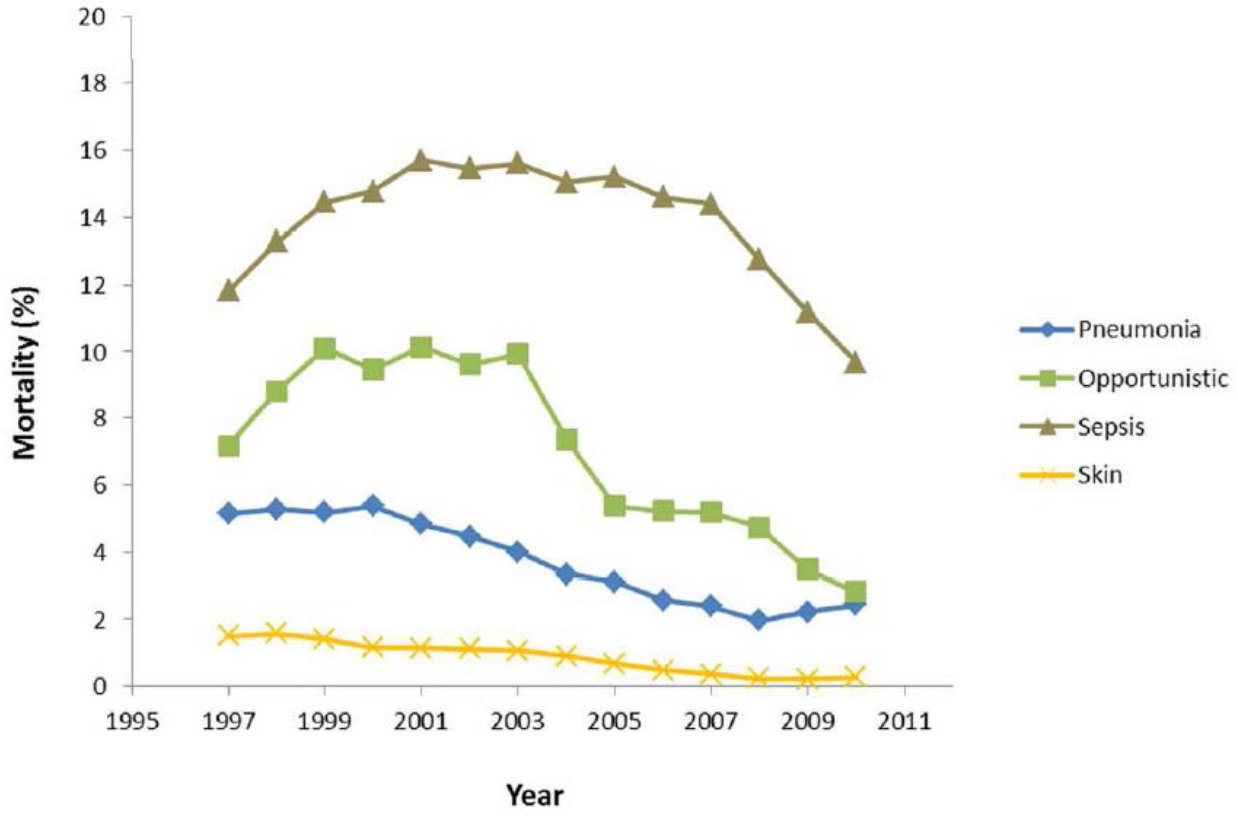


Tektonidou M et al, Arthritis Care & Res 2015 (in press)

In hospital mortality for infections in SLE patients

Compared to non-SLE pts

↑ mortality from opportunistic infections = 1.52 (1.12-2.07)



Tektonidou M et al, Arthritis Care & Res 2015 (in press)

What is the significance for our work?

Infections and rheumatic diseases

- The risk of reactivation in patients with past HBV infection treated with biologics is very low – No need for pre-emptive antiviral prophylaxis

- The new oral antivirals (DAAs) can cure >90% of HCV infected pts, although data in HCV-associated cryoglobulinemic vasculitis are missing

- The rate of flu (25-35%) and pneumo (<20%) vaccinations in rheum patients remains very low
  - HPV vaccine is safe and efficacious in young girls with JIA
  - HZ vaccine can be given in patients on DMARDs/low dose steroids and before starting biologics – Need more data on pts on chronic biologic therapy

- Think about Chikungunya virus related arthritis in recent travellers or migrants from endemic areas presenting with acute seronegative polyarthritis

What is the significance for our work?

Infections and rheumatic diseases

- - TB test conversion during anti-TNF therapy is not uncommon but its significance remains unclear

- There is a 30% increase in the rate of serious infections among RA patients receiving biologics compared to traditional DMARDs, which in absolute numbers equals to an increase from 2 to 2.6% per year

- The burden of serious infections and in hospital deaths have increased in SLE patients, emphasizing the need for aggressive vaccination and limitation of the use of glucocorticoids