JNI 20es Journées Nationales d'Infectiologie
Lyon
et la région Auvergne-Rhône-Alpes
du mercredi 5 juin 2019
au vendredi 7 juin 2019

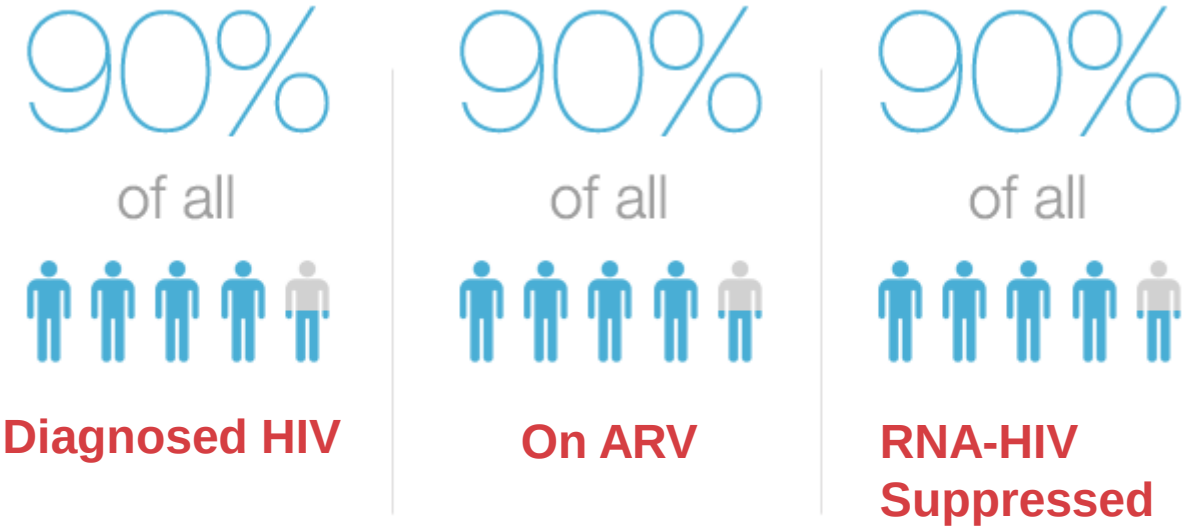
Bénéfices attendus d'un changement du traitement ARV: le long terme

Jean-Jacques Parienti, MD, PhD
CHU de Caen
Université Caen-Normandie

Conflicts of Interest

- **Grant support paid to my institution:**
  - MSD
  - ViiV
  - Gilead
- **Consulting/honorarium/travel grant:**
  - MSD
  - ViiV
  - Gilead

UNAIDS 90-90-90 goal



4th 90%

Beyond viral suppression of HIV – the new quality of life frontier

Jeffrey V. Lazarus[1,2*], Kelly Safreed-Harmon[2], Simon E. Barton[3], Dominique Costagliola[4], Nikos Dedes[5], Julia del Amo Valero[6], Jose M. Gatell[7], Ricardo Baptista-Leite[8,9], Luís Mendão[5], Kholoud Porter[10], Stefano Vella[11] and Jürgen Kurt Rockstroh[12]

Diagnosed HIV

On ARV

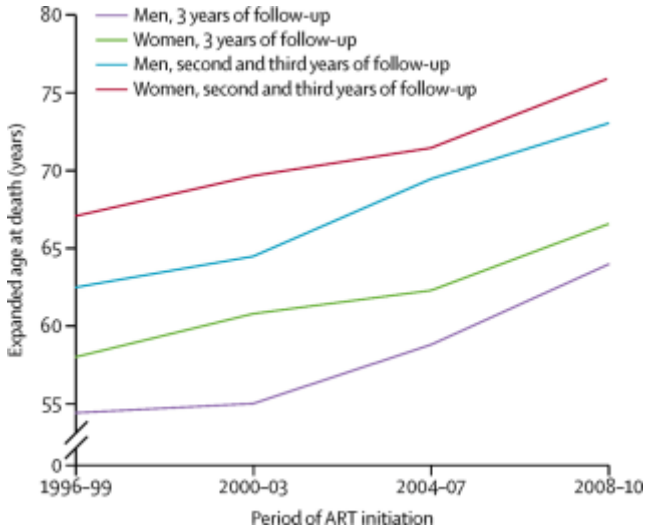
RNA-HIV Suppressed

Good health-related quality-of-life

Lazarus et al. BMC Med 2016

Life & QoL

Survival of HIV-positive patients starting antiretroviral therapy between 1996 and 2013: a collaborative analysis of cohort studies



ARV theray Cohort, Lancet HIV 2017

ASSESSMENT OF QUALITY-OF-LIFE OUTCOMES

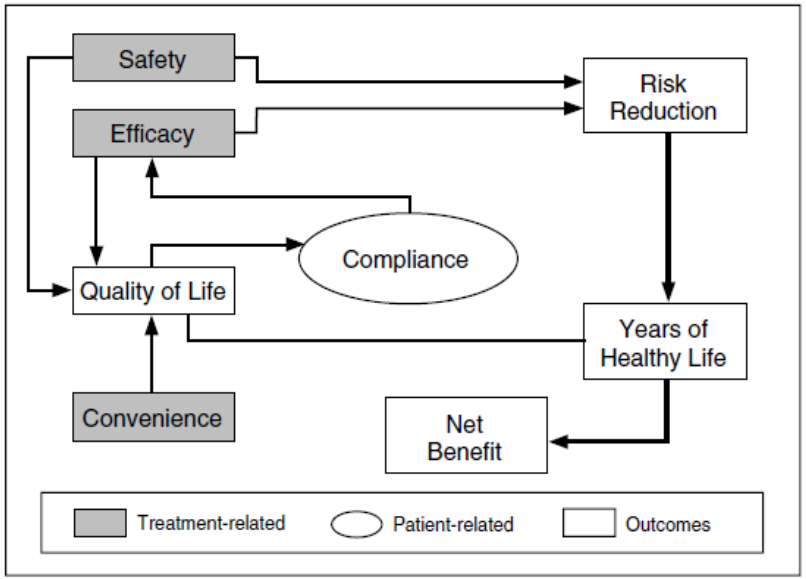


Figure 3. The Role of Quality of Life in Determining the Net Benefit of Therapy for a Chronic Disease.

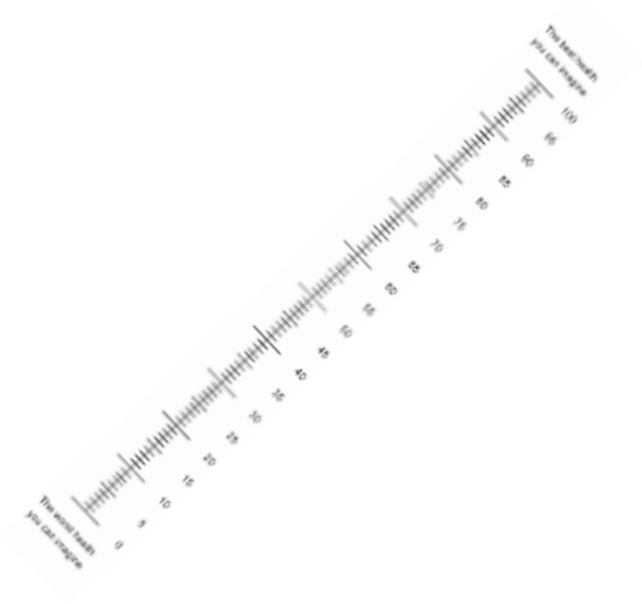
This hypothetical model shows the relations among treatment-related influences (safety, efficacy, and convenience), characteristics of patients (compliance), and measurable outcomes (quality of life, risk reduction, years of healthy life, and net benefit).

Testa M, N Engl J Med 1996

EQ-5D

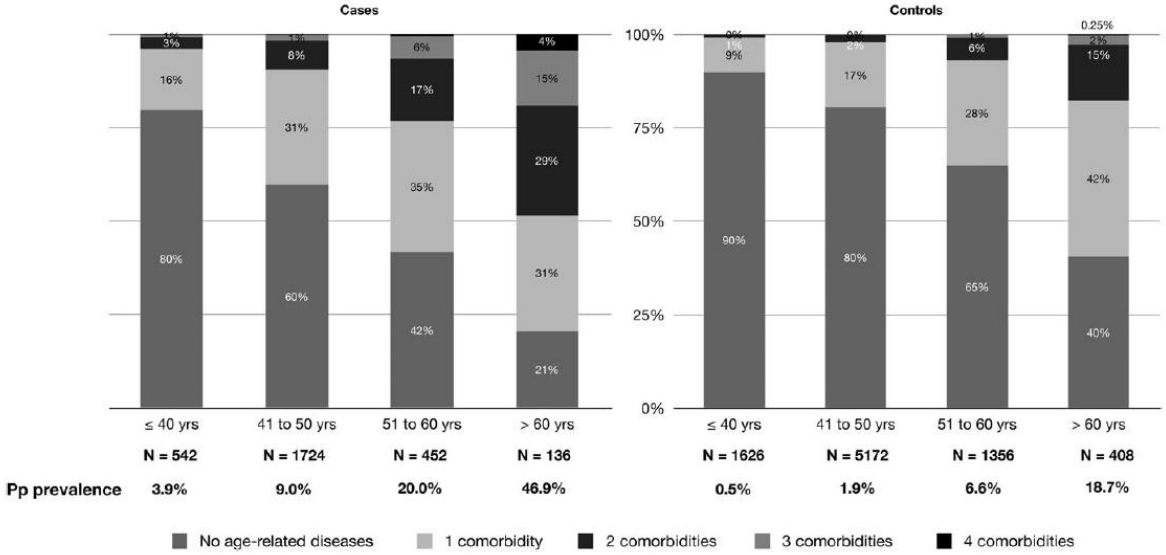
- **Descriptive system**
  - Mobility
  - self-care
  - usual activities
  - pain/discomfort
  - anxiety/depression

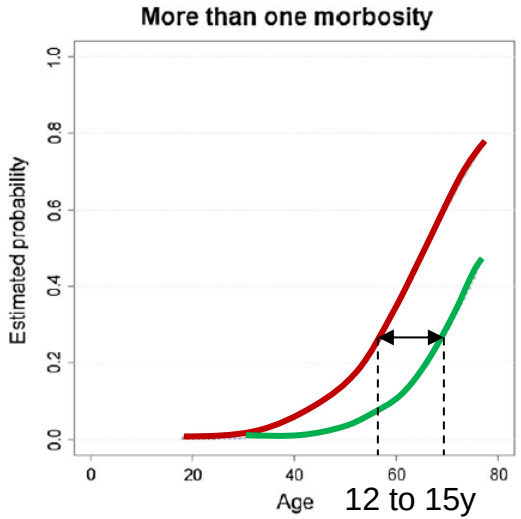
- **Visual analogue scale**



Premature Aging

Premature Age-Related Comorbidities Among HIV-Infected Persons Compared With the General Population

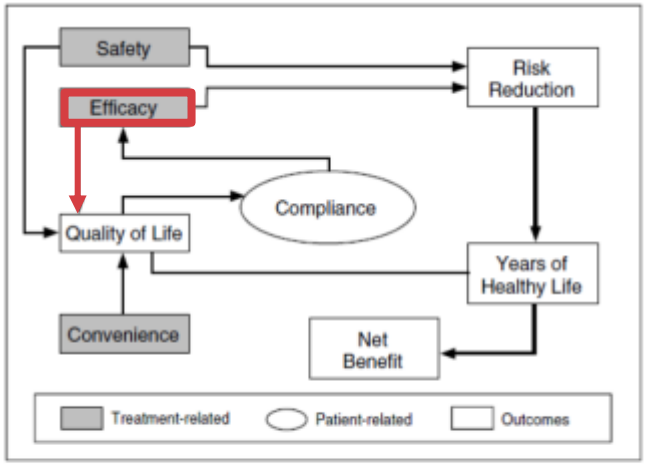




Guaraldi G. Clin Infect Dis 2011

Objectives of ARV modification

- **Maintain viral suppression**



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Testa M, N Engl J Med 1996

Maintain viral Suppression

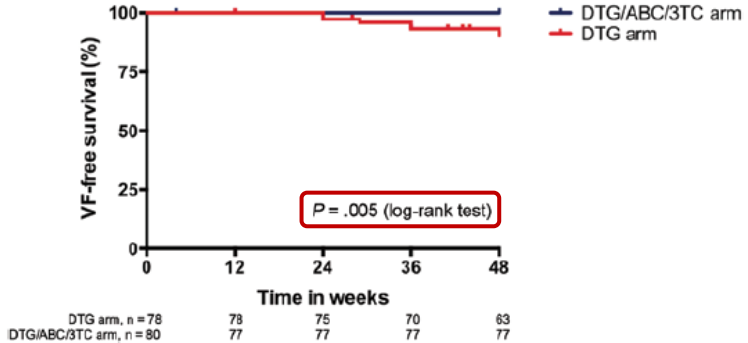
Switch to a raltegravir-based regimen versus continuation of a lopinavir-ritonavir-based regimen in stable HIV-infected patients with suppressed viraemia (SWITCHMRK 1 and 2): two multicentre, double-blind, randomised controlled trials

Investigator report of a history of previous virological failure†					
SWITCHMRK 1					
Yes	34/47	72·3% (57·4 to 84·4)	52/58	89·7% (78·8 to 96·1)	−17·3% (−33·0 to −2·5)
No	103/121	85·1% (77·5 to 90·9)	97/113	85·8% (78·0 to 91·7)	−0·7% (−9·9 to 8·6)
SWITCHMRK 2					
Yes	51/64	79·7% (67·8 to 88·7)	61/65	93·8% (85·0 to 98·3)	−14·2% (−26·5 to −2·6)
No	99/107	92·5% (85·8 to 96·7)	101/108	93·5% (87·1 to 97·4)	−1·0% (−8·5 to 6·3)

- Review Tx history
- Caution if prior Tx failures

Eron JJ, Lancet 2010

Dolutegravir Monotherapy Versus Dolutegravir/Abacavir/Lamivudine for Virologically Suppressed People Living With Chronic Human Immunodeficiency Virus Infection: The Randomized Noninferiority MONotherapy of TiviCAY Trial

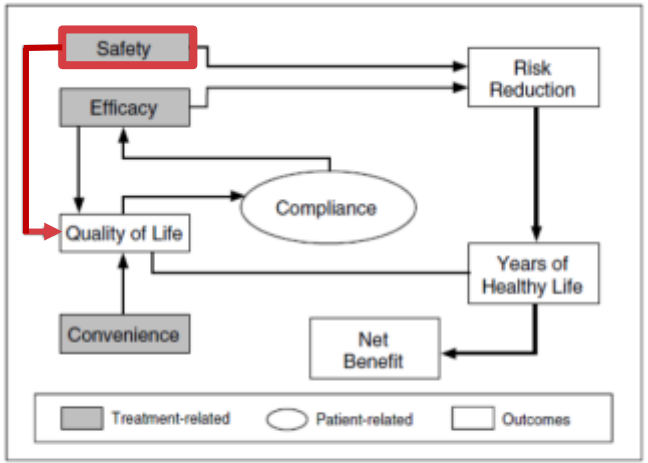


- Modify with recommended Tx

Hocqueloux L, Clin Infect Dis 2019

Objectives of ARV modification

- **Prevention of long-term toxicities**



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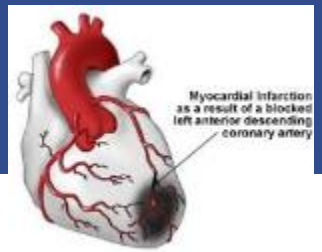
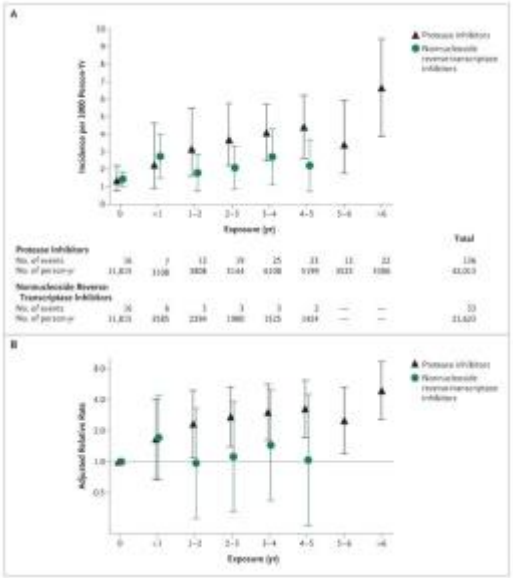
Testa M, N Engl J Med 1996

Myocardial infarction



- **High risk for PI in D:A:D**



DAD Study Group, NEJM 2007

- **ABC and MI is controversial**

Is there continued evidence for an association between abacavir usage and myocardial infarction risk in individuals with HIV? A cohort collaboration

Association between current use of ABC and MI risk

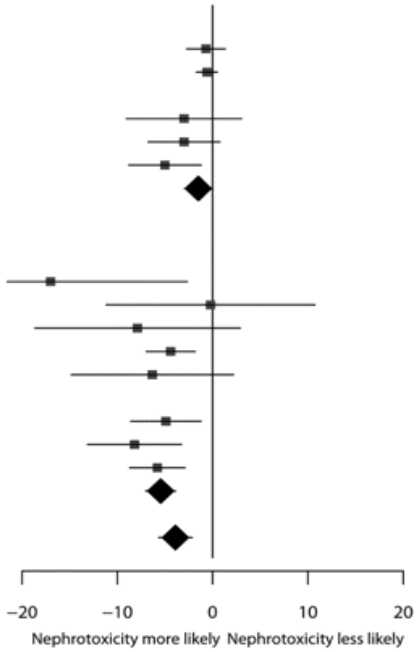
By 1 February 2013, 941 MI events had occurred in the cohort (rate 0.26 [95 % CI 0.24–0.27]/100 PYRS). Overall, the rate of MI was 0.47 [0.42–0.52]/100 PYRS among those currently receiving ABC and 0.21 [0.19–0.22]/100 PYRS among those not currently receiving ABC. After adjustment for potential confounders, current ABC use was associated with a 98 % increase in MI rate (aRR 1.98 [1.72–2.29]), with no difference in the pre- (1.97 [1.68–2.33]) and post- (1.97 [1.43–2.72]) March 2008 periods (*P* value for interaction = 0.74) (Table 3).

Sabin C, Plos Med 2016

Nephrotoxicity

- **Impact of TDF on eGFR in meta-analysis**

Study or subcategory	Total	MD [95% CI], mL/min
RCT		
ART naive		
BICOMBO 2009	333	−0.70 [−2.73, 1.33]
De Jesus 2009	300	−0.60 [−1.71, 0.51]
ART experienced		
HEAT 2009	672	−3.00 [−9.06, 3.06]
Arribas 2008	458	−3.00 [−6.77, 0.77]
Gallant 2004	600	−5.00 [−8.80, −1.20]
Subtotal		−1.50 [−2.96, −0.005]
Cohort		
ART naive		
Kinai 2009	63	−17.00 [−31.35, −2.65]
Goicoechea 2008 NNRTI	62	−0.22 [−11.18, 10.74]
Goicoechea 2008 RPI	84	−7.88 [−18.66, 2.90]
HOPS 2007	736	−4.40 [−6.97, −1.83]
Winston 2006	948	−6.33 [−14.85, 2.19]
ART experienced		
Fux 2007	284	−4.90 [−8.58, −1.22]
Fux 2007 N	569	−8.20 [−13.13, −3.27]
Gallant 2005	658	−5.80 [−8.70, −2.90]
Subtotal		−5.45 [−7.02, −3.89]
Total		−3.90 [−5.66, −2.14]



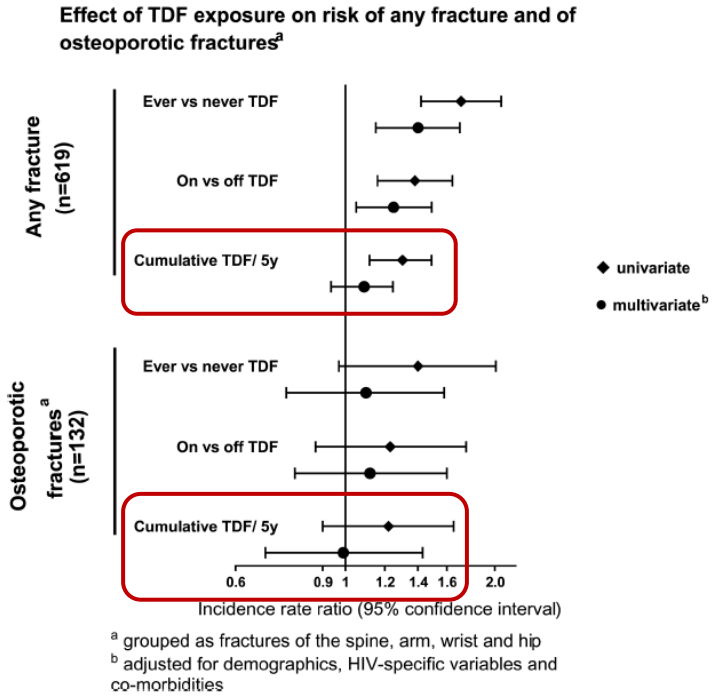
Cooper RD, Clin Infect Dis 2010

Bone Disease

Antiretrovirals, Fractures, and Osteonecrosis in a Large International HIV Cohort

- **TDF and osteoporotic fracture is controversial**

- **EuroSIDA cohort**
- **N=11,820 / 86,118 PYFU**
- **No dose-effect after adj.**

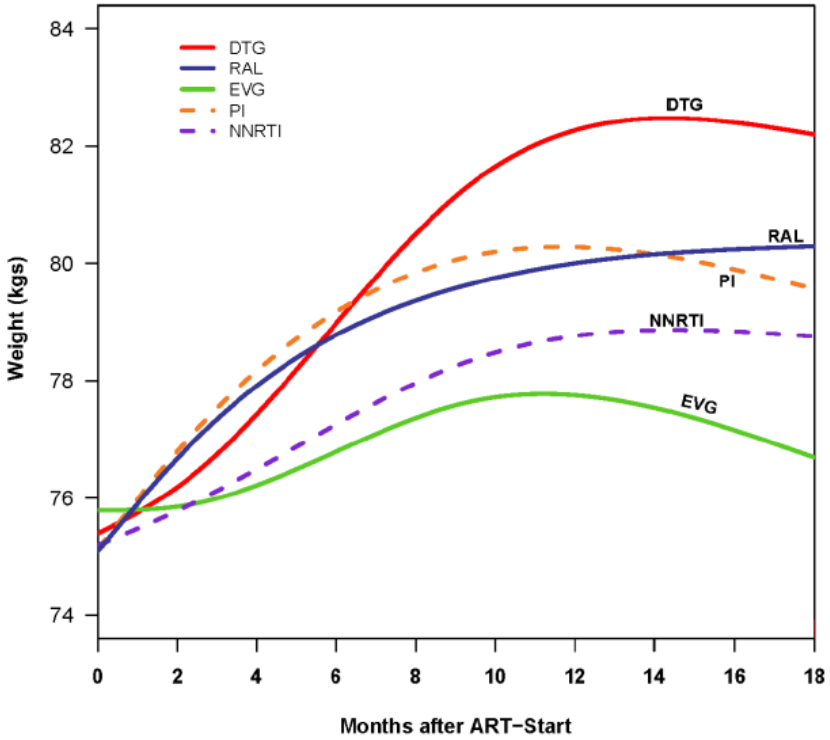


Borges A, Clin Infect Dis 2017

Weight gain

Greater Weight Gain in Treatment Naïve Persons Starting Dolutegravir-Based Antiretroviral Therapy

- Retrospective cohort, Nashville, US
- Only ART-naïve
- N=1,152
- +6.0 Kg at M18 w DTG



Bourgi K, Clin Infect Dis 2019

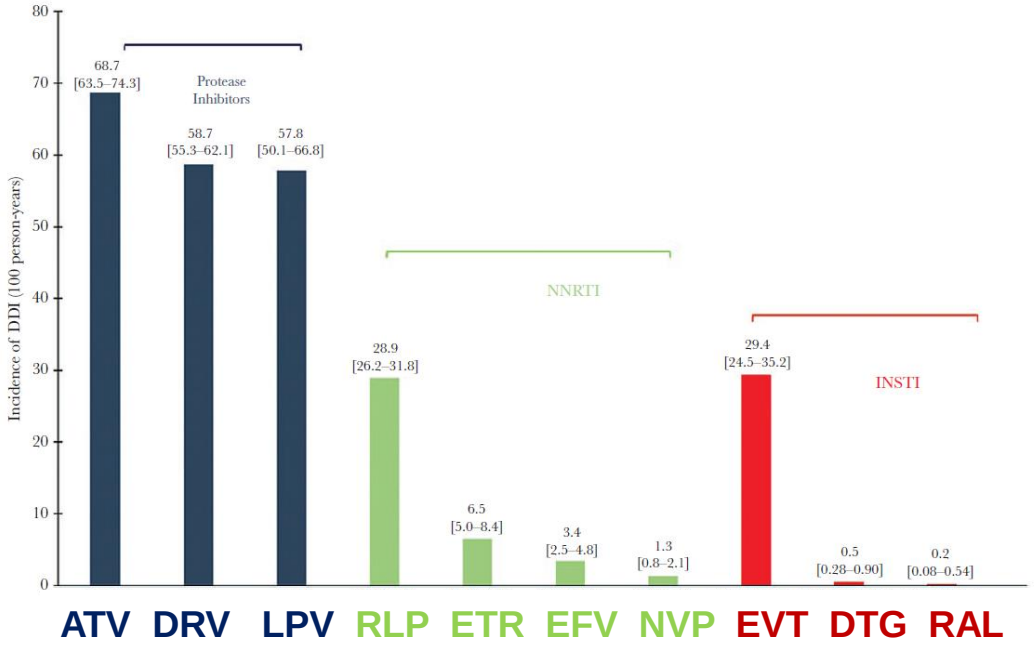
Pregnancy

ART Regimen Component Note: ARV drugs and ARV regimens are listed alphabetically within drug classes and recommendation categories	ART for Pregnant Women Who Have Never Received ARV Drugs and Who Are Initiating ART for the First Time	Continuing ART for Women Who Become Pregnant on an ART Regimen that has been Well Tolerated and Virologically Suppressive[a]	ART for Pregnant Women Who Have Received ARV Drugs in the Past and Who Are Restarting ART[b]	New ART Regimen for Pregnant Women Whose Current ART is not Well Tolerated and/or is not Resulting in Virologic Suppression[b]	ART for Nonpregnant Women Who Are Trying to Conceive[b,c]
NRTIs[d,e]					
ABC	Preferred	Continue	Preferred	Preferred	Preferred
FTC	Preferred	Continue	Preferred	Preferred	Preferred
3TC	Preferred	Continue	Preferred	Preferred	Preferred
TDF	Preferred	Continue	Preferred	Preferred	Preferred
ZDV	Alternative	Continue	Alternative	Alternative	Alternative
TAF	Insufficient data[f]	Continue	Insufficient data	Insufficient data	Insufficient data
INSTIs Used in combination with a dual-NRTI backbone[e]					
DTG These are interim recommendations, pending the availability of additional data.[g]	Not recommended during the first trimester[h] Preferred after the first trimester	Consider continuation with counseling or switch during the first trimester[g] Continue if patient is in the second or third trimester	Not recommended during the first trimester[g] Preferred after the first trimester	Not recommended during the first trimester[g] Preferred after the first trimester	Not recommended[g]
RAL	Preferred	Continue	Preferred	Preferred	Preferred
BIC	Insufficient data	Insufficient data	Insufficient data	Insufficient data	Insufficient data
EVG/COBI	Not recommended[h]	Consider switch, or continue with frequent viral load monitoring[i]	Not recommended[h]	Not recommended[h]	Not recommended[h]
PIs Used in combination with a dual-NRTI backbone[e]					
ATV/r	Preferred	Continue	Preferred	Preferred	Preferred
DRV/r	Preferred	Continue	Preferred	Preferred	Preferred
LPV/r	Alternative	Continue	Alternative	Alternative	Alternative
ATV/COBI	Not recommended[h]	Consider altering the regimen, or continuing the same regimen with frequent viral load monitoring[i]	Not recommended[h]	Not recommended[h]	Not recommended[h]
DRV/COBI	Not recommended[h]	Consider altering the regimen, or continuing the same regimen with frequent viral load monitoring[i]	Not recommended[h]	Not recommended[h]	Not recommended[h]

Serious Drug-Drug Interaction

Risk and Cost Associated With Drug–Drug Interactions Among Aging HIV Patients Receiving Combined Antiretroviral Therapy in France

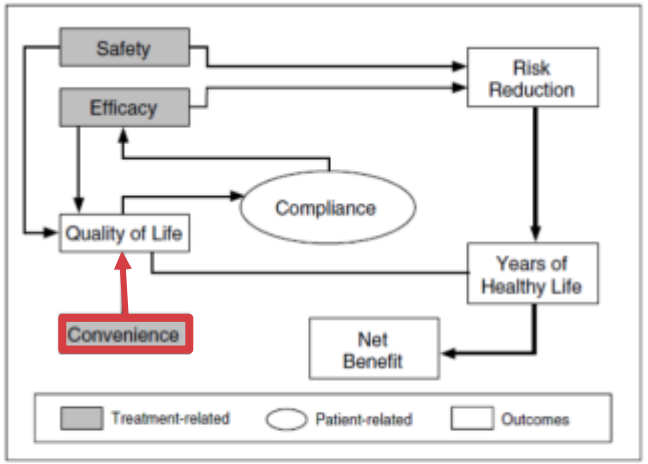
- SNIIRAM database
- Prospective cohort >65yo, 1y F/up
- N=9076
- 17% of serious DDIs
- +2700€/y



Demessine L, Open Forum Infect Dis 2019

Objectives of ARV modification

- **Simplify**



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Testa M, N Engl J Med 1996

Adherence

Better Adherence with Once-Daily Antiretroviral Regimens: A Meta-Analysis

Jean-Jacques Parienti,[1,2,3,4] David R. Bangsberg,[5] Renaud Verdon,[2] and Edward M. Gardner[6]

Study or Subgroup	Once-daily Mean	SD	Total	Twice-daily Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Treatment switch studies								
Benson 2004	90	18.3	294	90	17.2	146	10.3%	0.00 [-3.49, 3.49]
Boyle 2008	87.1	31	205	77.1	31	95	4.5%	10.00 [2.46, 17.54]
Parienti 2007	95	6.2	27	93.3	8.3	25	9.3%	1.70 [-2.31, 5.71]
Porthsmouth 2005	96.1	3.6	22	95.8	3.1	21	13.5%	0.30 [-1.71, 2.31]
Ruane 2006	85.4	9.1	18	84.4	12	13	4.3%	1.00 [-6.76, 8.76]
Sosa 2005	93	18.3	119	93	17.2	117	8.3%	0.00 [-4.53, 4.53]
Subtotal (95% CI)			**685**			**417**	**50.4%**	**1.00 [-0.84, 2.84]**
Heterogeneity: Tau² = 1.21; Chi² = 6.47, df = 5 (P = 0.26); I² = 23%								
Test for overall effect: Z = 1.06 (P = 0.29)								
Treatment naive studies								
Eron 2004	94	18.3	19	92	17.2	19	2.4%	2.00 [-9.29, 13.29]
Gallant 2006	90	11.7	244	87	14	243	12.9%	3.00 [0.71, 5.29]
Kubota 2006	94.3	15.8	411	92.9	15.7	195	12.1%	1.40 [-1.28, 4.08]
Molina 2007	99.8	11	115	92.6	9.4	75	11.5%	7.20 [4.27, 10.13]
Rode 2008	90.8	20.7	310	83.8	20.7	296	10.7%	7.00 [3.70, 10.30]
Subtotal (95% CI)			**1099**			**828**	**49.6%**	**4.40 [1.81, 6.99]**
Heterogeneity: Tau² = 5.28; Chi² = 12.19, df = 4 (P = 0.02); I² = 67%								
Test for overall effect: Z = 3.33 (P = 0.0009)								
Total (95% CI)			**1784**			**1245**	**100.0%**	**2.88 [0.98, 4.78]**
Heterogeneity: Tau² = 5.89; Chi² = 29.74, df = 10 (P = 0.0009); I² = 66%								
Test for overall effect: Z = 2.99 (P = 0.003)								
Test for subgroup differences: Chi² = 11.07, df = 1 (P = 0.0009), I² = 91.0%								

Mean Difference IV, Random, 95% CI

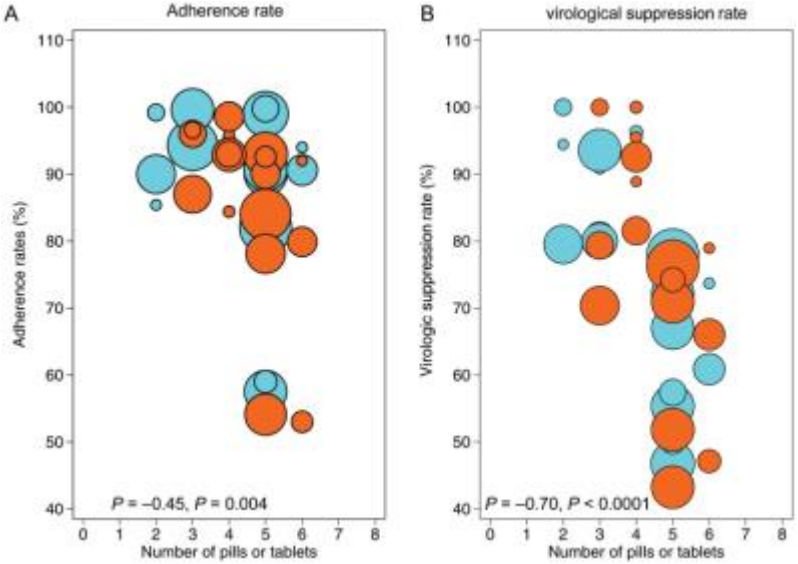
-10 -5 0 5 10

Favours experimental Favours control

Adapted from Parienti JJ et al., Clin Infect Dis 2009

Lower Pill Burden and Once-Daily Antiretroviral Treatment Regimens for HIV Infection: A Meta-Analysis of Randomized Controlled Trials

Jean B. Nachega,[1,2,3,4,a] Jean-Jacques Parienti,[5,6,a] Olalekan A. Uthman,[7,8,9] Robert Gross,[10] David W. Dowdy,[2] Paul E. Sax,[11] Joel E. Gallant,[12] Michael J. Mugavero,[13] Edward J. Mills,[14] and Thomas P. Giordano[15]



Parienti JJ et al., Clin Infect Dis 2014

Conclusion

- Close monitoring of ARV toxicity
- In some situations, switch now to prevent future complications (d4T, AZT, TDF if prior CKD or low eGFR, ABC if high CV risk)
- Check for DDIs regularly
- Long-term complications are unknown for new drugs

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- Anne Martin
- Fabien Chaillot
- Pascale Goubin
- Philippe Feret
- Jean-Jacques Dutheil

Co-Med Week

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SUIVIS EN ***CONSULTATION***

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