
Respect


Qualité


Solidarité


Innovatie


Engagement

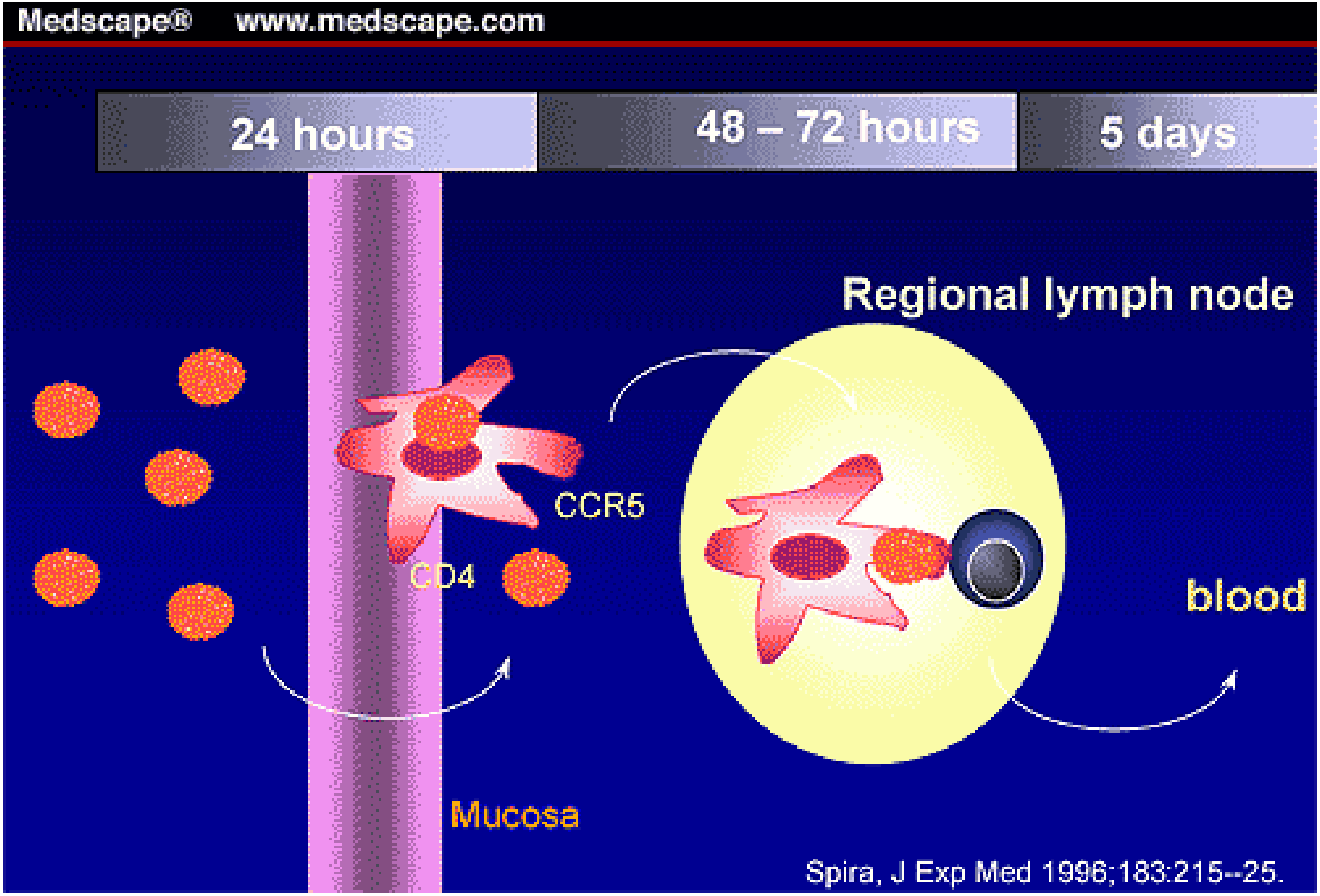
NONOPEP in Belgium

Dr Agnès Libois
CHU Saint-Pierre
25-11-2016

NONOPEP= non-occupational post-exposure prophylaxis

Plan

- The first years of NONOPEP
- New convention
- New guidelines
- Results of the Saint-Pierre cohort


Medscape® www.medscape.com
24 hours
48 – 72 hours
5 days
Regional lymph node
CCR5
CD4
blood
Mucosa
Spira, J Exp Med 1996;183:215--25.

Factors justify the administration of NONOPEP

1. A biological plausibility of PEP for preventing HIV infection (48 h to 72 h to become detectable in regional lymph nodes and 5 days to disseminate in blood)
2. The effectiveness of PEP in animal studies (<72h, 28 days)
3. The effectiveness of OPEP in humans

   (AZT after needle-stick exposures reduced risk of seroconversion for HIV by 81%)
4. Efficacy in the prevention of mother to child HIV transmission

NONOPEP « old convention »

- AR of june 2009: INAMI/RIZIV special fund pay for NONOPEP if:
  - prescribed by a AIDS reference center
  - indication follow belgian guidelines
  - No other insurance
- 882.52 euros+ 150 euros for administrative costs= **1032,52** euros/patient.

New convention (1)

- In 2016 but with retroactive effect from januari 2013
- Accidental exposure: unintended, unpredictable….
- If occupational exposure, the professional has to declare that he/she has no other insurance

New convention (2)

- 653,17 euros (including administrative costs) → - 37%
- Inform consent
- Data collection in collaboration with IPH (without additional financial support)

New Belgian Guidelines 2016 (1)

- Inspired by the UK guideline 2015 and the former Belgian guideline.
- Initiation of NONOPEP is recommended as soon as possible after exposure, preferably within 24 h of exposure but can be offered up to 72 h.
- The duration of NONOPEP should be 28 days.

Cresswell F. UK guideline for the use of HIV Post-Exposure Prophylaxis Following Sexual Exposure, 2015. Int J STD AIDS. 2016

New Belgian Guidelines 2016 (2)

- Decisions whether or not to start prophylaxis should be taken **on a case by case** basis, taking into account the kind of individual risk the patient has taken and factors increasing the risk of transmission.

What is new?

- Not recommended if the source is on ART with a confirmed and sustained (>6 months) undetectable plasma HIV VL (<200 c/mL).
- Not-recommended following fellatio-with ejaculation as the risk is <1/10.000:
  - estimated risk in modeling studies: 4/10.000
  - In a cohort study, no seroconversion after 19.000 unprotected orogenital exposures with an HIV-positive partner
  - If suspicion of primary infection in the source and oropharyngeal trauma, NONOPEP can be considered.

Vittinghoff E. Am J Epidemiol 1999, del Romero J. AIDS 2002

- Recommend when there is a significant risk of HIV transmission risk>1/1.000
- Consider if the transmission risk is between 1 in 1.000 and 1 in 10.000
- Not recommended if the transmission risk is < 1/10.000

Risk of HIV transmission=
risk that source is HIV positive
x risk per exposure

1. Evaluate the risk of transmission: Estimated HIV prevalence in Belgium

- MSM:
  - 5% in general gay venues in Flanders, 9% in Brussels
  - 14.5% in high risk venues (cruising)
- Female sex workers:
  - <1% in Western Europe
  - 1-2% in Central Europe
  - 2.5-8% in Eastern Europe
- Male sex workers: 14%
- African heterosexual: Congolese 2%
- Prevalence in the general population 0.1 to 0.2%.

HIV prevalence in other countries can be found in the UNAIDS Gap report

Vanden Berghe W. A venue-based HIV prevalence and behavioural study among men who have sex with men in Antwerp and Ghent, Flanders, Belgium, October 2009 to March 2010. Euro Surveill. 2011.

2.Evaluated the risk per exposure

Type of exposure	Estimated risk of HIV transmission per exposure from a known HIV-positive individual not on ART	References
Receptive anal intercourse	1 in 90	(4-10)
Receptiveanal intercourse with ejaculation	1 in 65	(4-11)
Receptive anal intercourse no ejaculation	1 in 170	(11)
Insertive anal intercourse	1 in 666	(4, 6, 7, 12)
Insertive anal intercourse not circumcised	1 in 161	(11)
Insertive anal intercourse and circumcised	1 in 909	(11)
Receptive vaginal intercourse	1 in 1000	(4, 9, 13-19)
Insertive vaginal intercourse	1 in 1219	(8, 9, 13-19)
Semen splash to eye	<1 in 10, 000	(20)
Receptive oral sex (giving fellatio)	< 1 in 10,000	(7, 14, 19, 21)
Insertive oral sex (receiving fellatio)	< 1 in 10,000	(6, 19)
Blood transfusion (one unit)	1 in 1	(22)
Needlestick injury	1 in 333	(21, 23, 24)
Sharing injecting equipment (includes chemsex)	1 in 149	(20)
Human bite	< 1 in 10,000	(25, 26)

Examples

- MSM presents for NONOPEP following unprotected receptive anal intercourse with ejaculation with male partner of unknown HIV status in Brussels:

  Risk of HIV transmission=

  prevalence in MSM in Brussels (9/100) x estimated risk (1/65) = 9/6500= 1/722

  → recommended

Examples

- MSM with insertive anal sex with MSM of unknown status :

  14.5/ 100 X 1/666 = 14.5/ 66600=

  1/4593 → consider
- Receptive vaginal sex with black malawi with unknown status :

  10.3 /100 X 1/1000 = 10.3/100000=

  1/9708 → consider

Examples

- Receptive vaginal sex with black congelese with unknown status:

  Prevalence in Congo is 2/100 x 1/1000= 2/100000= 1/50000 → rather not recommended

However, some factors may increase the risk of HIV transmission and must be considered

BOX 1 Factors increasing the risk of HIV transmission:

1. A high plasma VL in the source, particularly during primary HIV infection
2. Breaches in the mucosal barrier: ulcer, trauma following sexual assault or first intercourse
3. Menstruation or other bleeding (theoretical risk only)
4. Sexually Transmitted Infection
5. Ejaculation
6. Non-circumcision

The final decision whether or not to start/continue prophylaxis will be taken by the doctor **on a case by case** basis.

	HIV positive with unknown/detectable viral load	HIV positive treated with viral load <200 copies/ml	Unknown HIV status From high risk/prevalence group[2] or high risk area[3]	Unknown HIV status From low risk/prevalence group[2] or low risk area[3]	Rape (except if condom used or rapist with proven recent negative HIV status)
RECEPTIVE ANAL	Recommend	Not recommended [1]	Recommend	Not recommended	Recommend
INSERTIVE ANAL	Recommend	Not recommended	Consider	Not recommended	NA
RECEPTIVE VAGINAL	Recommend	Not recommended	Consider	Not recommended	Consider
INSERTIVE VAGINAL	Recommend	Not recommended	Consider	Not recommended	NA
RECEPTIVE ORAL WITH EJACULATION	Not recommended except if cofactors 1 and 2 (see Box1)	Not recommended	Not recommended except if cofactors 1 and 2 (see Box 1)	Not recommended	Not recommended except if cofactors 1 and 2 (see Box 1)
RECEPTIVE ORAL WITHOUT EJACULATION	Not recommended except if cofactors 1 and 2 (see Box1)	Not recommended	Not recommended except if cofactors 1 and 2(see Box 1)	Not recommended	Not recommended except if cofactors 1 and 2(see Box 1)
SHARING OR INJECTING EQUIPMENT	Recommend	Not recommended	Recommend	Not recommended	

Others situation:

- **Needlestick from a discarded needle in the community: not recommended**
- Not recommended in case of oral insertive sex, cunnilungus or following semen splash in the eye as there have been no documented HIV transmissions via this route
- Aggression with a needlestick: consider if visible blood, deep injury
- Human bite: generally not recommended, consider if blood in the mouth of assaulter
- Blood on non intact skin/mucosal: consider

Which regimen?

- First choice:

Truvada + Tivicay or Truvada+Isentress.

  - well tolerated,
  - high levels of adherence
  - avoid potential drug-drug interactions
  - recommended by the vast majority of recent guidelines from other countries (CDC, UK, Holland,…).

But not affordable with the current RIZIV/INAMI convention…

Medication regimen

- Genvoya ® (EVG/FTC/TAF/COB) or Stribild ® (EVG/FTC/TDF/COB) may be considered as an alternative but drug-drug interactions are a concern in the NONOPEP target population (recreational drug, ….)

But not affordable with the current RIZIV/INAMI convention…

Regimen possible in the convention:

- Combivir 2x/j + Crixivan 400 2x/r
- Zerit+epivir Kaletra 2x2

  Reyataz 400 mg (2 comp)
- But lot of side effects: asthenia, digestive, unable to work, …

Regimen possible in the convention:

- Result in poor levels of adherence:

  60% for Zerit-Epivir-Kaletra in the Saint-Pierre Cohort vs 96% in a French study with Truvada and Isentress.
- potential drug-drug interaction with the regular treatment of the patient and with recreational drug (used frequently among MSM).

Malinverni S, Libois A, Gennotte AF, La Morté C, Mols P. PLOS ONE 2016
S. Henard et al, 14th EACS European AIDS Clinical Society Conference, 2013 Brussels,PE18/1

PLOS | ONE

RESEARCH ARTICLE

Prescription of Non-Occupational Post-Exposure HIV Prophylaxis by Emergency Physicians: An Analysis on Accuracy of Prescription and Compliance

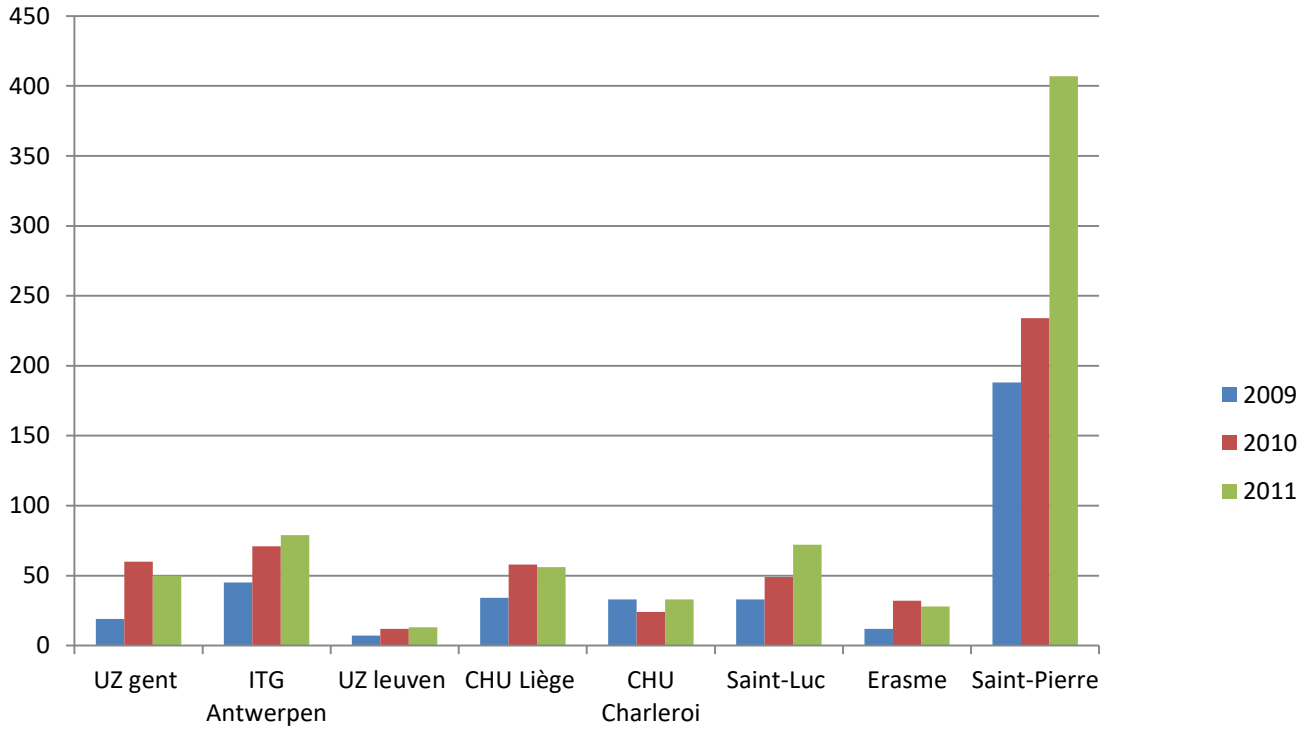
Stefano Malinverni[1]*, Agnès Libois[2☯], Anne-Françoise Gennotte[2☯], Cécile La Morté[2☯], Pierre Mols[1☯]

2016. 11(4): e0153021. doi:10.1371/journal.pone.0153021

- One center, Brussels, Belgium.
- 1,357 cases consulting from 01/2011 to 12/2013 $\rightarrow \cong$ 450 cases/year
- Retrospective analysis of data from a prospective nPEP registry
- Regimen: Kaletra-Zerit-Epivir

Malinverni S et al. PlosOne 2016

Number of NONOPEP in Belgium: 2009-2011



Objectives:

- To determine whether emergency physicians prescribe nPEP according to national guideline with support from IDS (infectious disease specialists).
- To measure compliance to nPEP
- To describe the population consulting for nPEP at our center

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Results (1)

- 96% sexual exposure
- 72% male
- 37% MSM/5% Bi
- 76% health insurance
- 53% non Belgian
- 12% multiple NONOPEP demands
- 15% sexual assaults

Malinverni S et al. PlosOne 2016

Results (2)

- Unprotected receptive anal: 25%
- Unprotected insertive anal:19%
- Unprotected vaginal receptive 26%
- >1 type of exposure 32%
- 17% of source persons were known HIV-infected

Malinverni S et al. PlosOne 2016

Results (3)

- 1357 demands, nPEP prescribed in 947 (69%) cases
- Emergency physicians prescribed nPEP
  - in 98.6% of high risk exposures
  - in 53.2% of intermediate risk exposures

  → Emergency physicians can safely and adequately prescribe nPEP when supported by a comprehensive guideline

Malinverni S et al. PlosOne 2016

Results (4)

- Compliance 60% (65% in a meta-analyse (*Ford AIDS 2014*))
- Compliance in MSM 67%
- Compliance in sexual assault victims: 40%
- 20% didn’t attend the first follow-up visit

Malinverni S et al. PlosOne 2016

Results (5)

- One episode of seroconversion at 4 months post-exposure in a MSM having had URAI with a HIV positive source and having received a complete nPEP regimen without reporting successive at risk behaviours.

Malinverni S et al. PlosOne 2016

- Following these results our centre changed the regimen for sexual assault victims into Stribild ® as a measure to simplify drug regimen and improve compliance

Malinverni S et al. PlosOne 2016

Compliance of fixed dose single tablet EVG/COBI/FTC/TDF (Stribild®) regimen vs LPV/r /d4T/3TC for PEP in sexual assault victims. A retrospective sequential period study.

Glasgow 2016 P010

Stefano Malinverni*, Agnès Libois, Pierre Mols*, Stéphane De Wit
Saint-Pierre University hospital, Division of infectious diseases and Emergency Department*, Brussels, Belgium.
E-mail : maladiesinfectieuses@stpierre-bru.be

CHU Saint-Pierre UMC Sint-Pieter

ULB

- Retrospective sequential period analysis between January 2011 and December 2015
- Persons consulting at our institution for PEP following sexual assault.
- Data extracted from a prospective PEP registry
- Patients receiving 28 days of treatment were considered compliant.

Glasgow
2016
P010

Compliance of fixed dose single tablet EVG/COBI/FTC/TDF (Stribild®) regimen vs LPV/r /d4T/3TC for PEP in sexual assault victims. A retrospective sequential period study.

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E-mail : maladiesinfectieuses@stpierre-bru.be

CHU Saint-Pierre
UMC Sint-Pieter

ULB

- 368 cases consulted→ 283 received PEP
- 91% female
- Mean age : 27 years
- 50% migrant

Malinverni S et al. PlosOne 2016

Glasgow
2016
P010

Compliance of fixed dose single tablet EVG/COBI/FTC/TDF (Stribild®) regimen vs LPV/r /d4T/3TC for PEP in sexual assault victims. A retrospective sequential period study.

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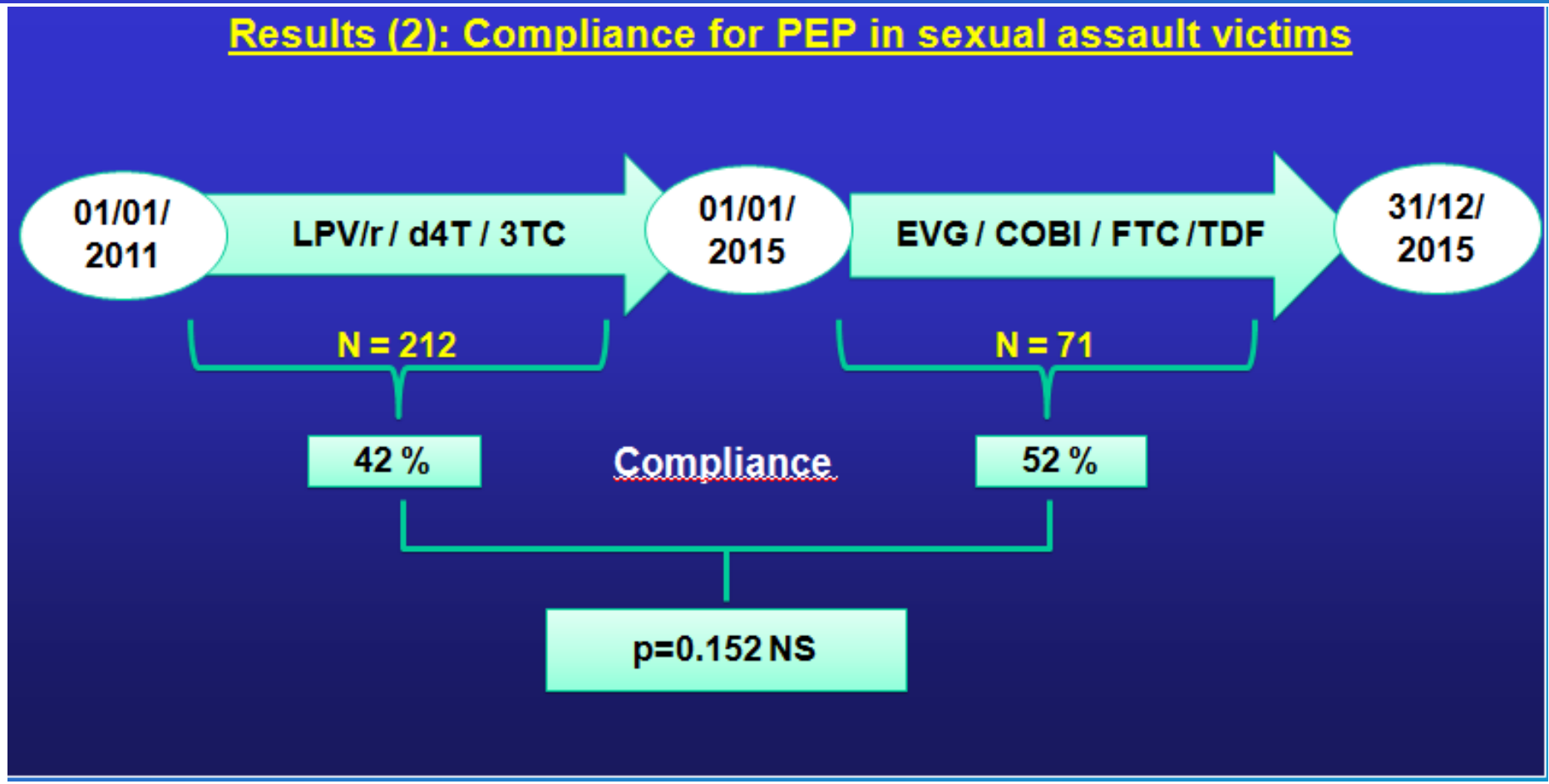
Results (2): Compliance for PEP in sexual assault victims



Switching to a well tolerated single pill regimen (EVG/COBI/FTC/TDF) modestly improve compliance suggesting that in sexual assault victims other drug regimens and other interventions should be implemented

Take home messages

- New convention with less money
- New guideline with
  - more restricted NONOPEP indication
  - Estimated risk, more « rational»
- Compliance problem with « old, cheaper ART »
- Other compliance problem in rape