



Georgia Department of Public Health

Clinical Aspects of Prescribing and Monitoring Patients on PrEP

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Disclosure

I have no vested interests that relate to this presentation

Nor do I have any relationships with;
pharmaceutical companies
biomedical device manufacturers
and/or other corporations

Whose products or services are related
to pertinent therapeutic areas

Learning Objectives

- Discuss: importance of a comprehensive prevention plan
- Discuss: preventing HIV through pre-exposure prophylaxis
- Understand: the importance of adherence
- Describe: PrEP in the context of a comprehensive plan

Where Does Prevention Fit?

Minimize Exposure



Testing
Condoms
TasP
Low Risk Sex
Needle exchange



Ms. Jones

32yo TG Woman calls her PCP to request an appointment to discuss PrEP and requests that her fiancée, a 33yo gentleman who was informed by a local clinic 6 months ago that he had HIV, accompany her during the appointment.

The front desk staff inform Ms. Jones that only family can be in the room during the appointment with the provider.

Should Ms. Jones schedule the appointment?

Changing Providers

Ms. Jones goes to www.gacapus.com and is linked to an HIV specialist and schedules an appointment to discuss PrEP. Ms. Jones' fiancée presents with her and brings his records.

Fiancée: HIV positive, CD4 350, HIV-VL >100,000

The couple states that condoms are used on occasion and that her HIV test was negative 3 months ago - records unavailable

What should NOT be done during this visit?

- A discussion on more consistent condom use
- A discussion on getting the fiancée into care and on HAART
- Getting Ms. Jones retested for HIV
- Starting PrEP on today's visit

TREATMENT IS PREVENTION

A scientific breakthrough in 2011 showed that HIV treatment not only saves lives, but reduces the risk by

96%

of transmitting the disease.

Results & Conclusions

39 HIV-1 observed transmissions

28 virologically linked to partner

1 occurred in early-therapy group

The early initiation of antiretroviral therapy reduced rates of sexual transmission of HIV-1 and clinical events, indicating both personal and public health benefits from such therapy

http://www.hptn.org/research_studies/hptn052.asp

Target 2020

90%

of all



living with HIV will
know their HIV
status

90%

of all



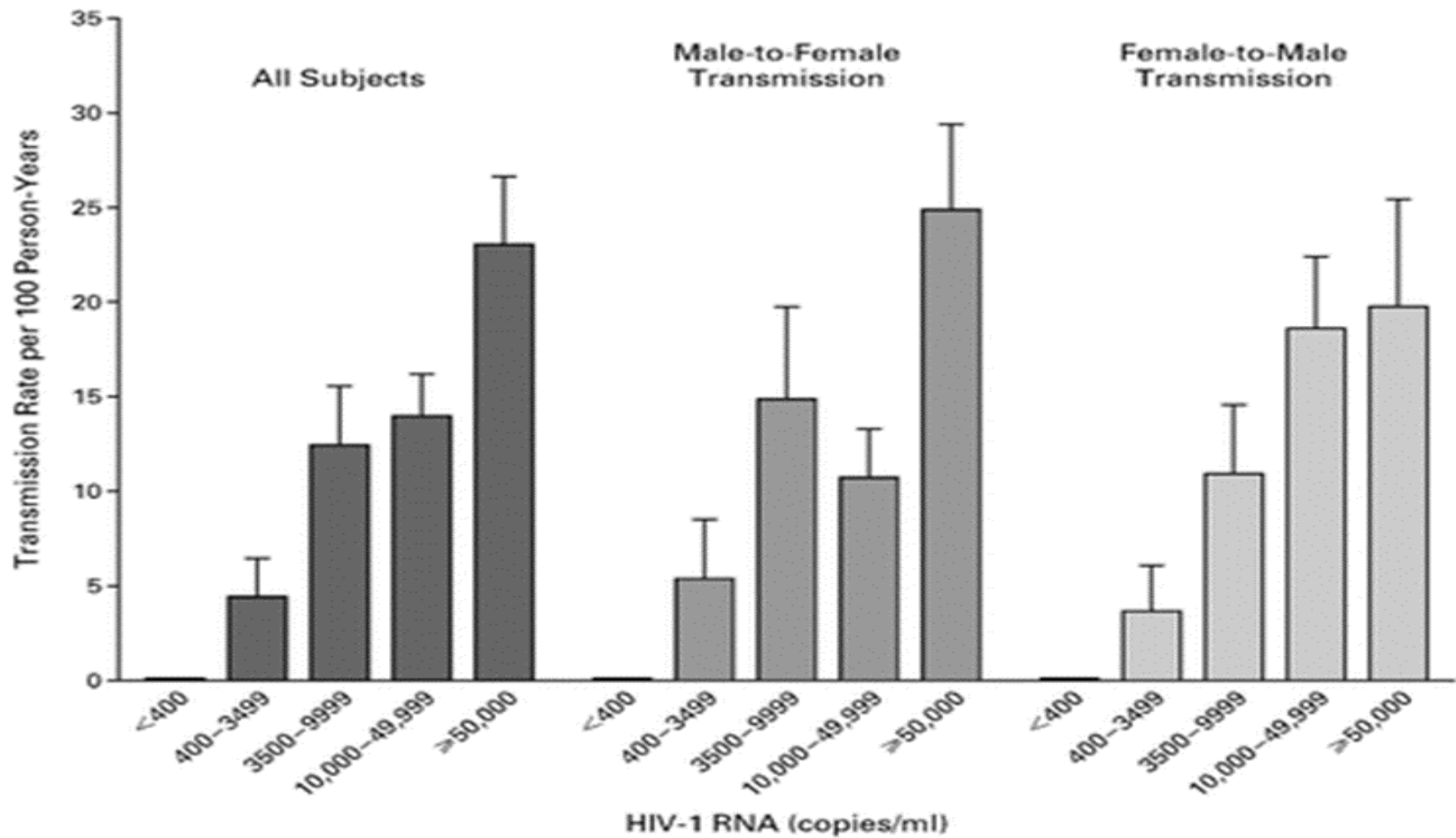
living with HIV will
receive sustained
antiretroviral
therapy

90%

of all

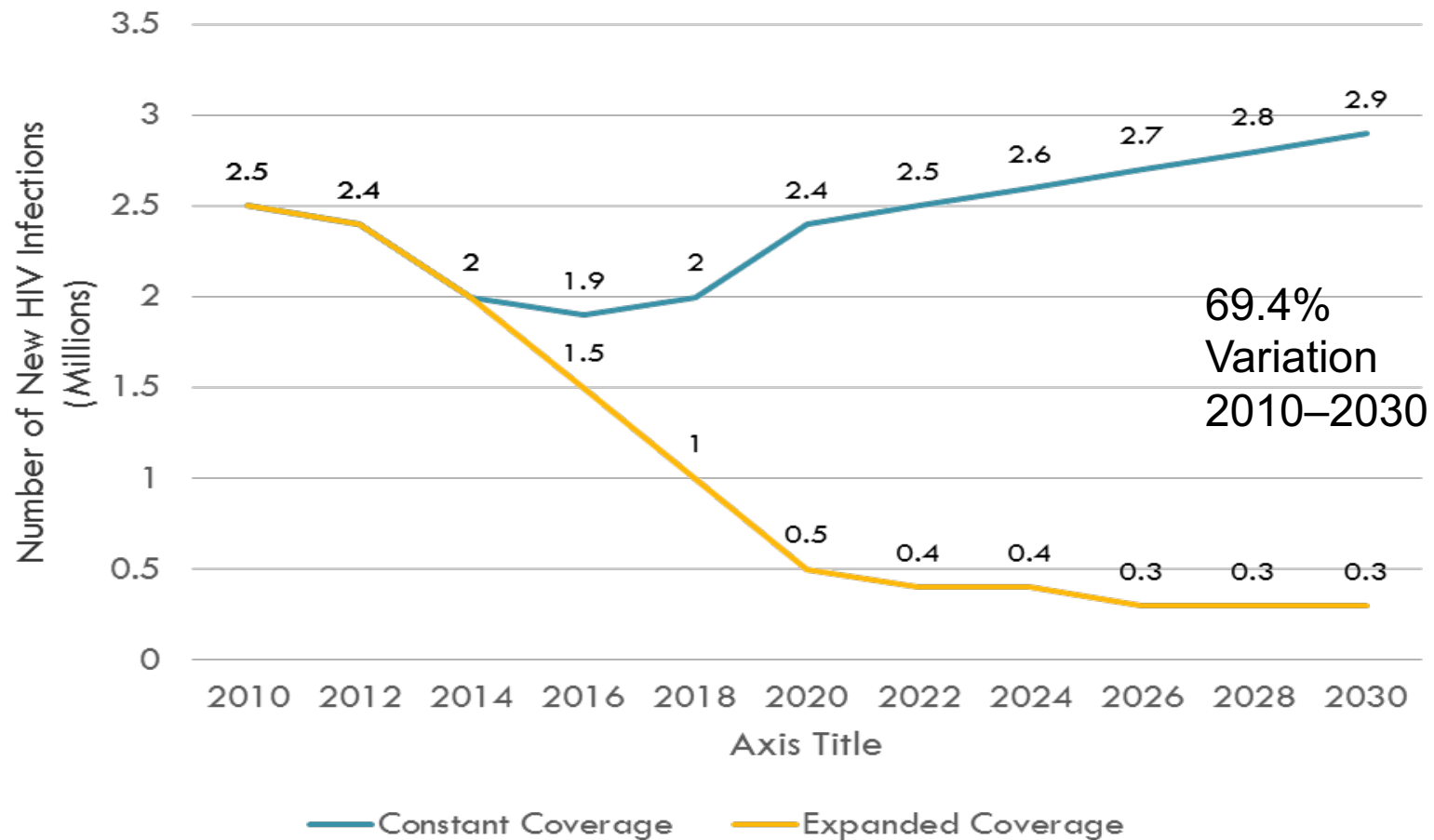


receiving
antiretroviral therapy
will have durable viral
suppression



<http://www.nejm.org/doi/full/10.1056/NEJM200003303421303>

Ending AIDS Scenario: New HIV Infections (2010-2030)



Source: UNAIDS 2014 estimates

Ms. Jones

Ms. Jones' fiancée enters into care and started on a single tab regimen with follow up labs demonstrating a CD4 550 and an HIV-VL of < 75.

Ms. Jones states that condoms are almost always used and she has undergone further evaluation with a negative recent HIV study.

PrEP is initiated.

How many days of PrEP should Ms. Jones receive on today's visit?

- 30 day supply
- 60 day supply
- 90 day supply
- 180 day supply

Pre-Exposure Prophylaxis (PrEP)

- HIV prevention strategy
- HIV-negative individuals
 - take anti-HIV medications
 - before contact with HIV
 - reduce risk of infection
- Medications work
 - prevent HIV
 - from establishing infection

iPrEx study

- Take 7 pills per week
 - est. protection: 99%
- Take 4 pills per week
 - est. protection: 96%
- Take 2 pills per week
 - est. protection: 76%

Adherence is Key

Trial	Efficacy	Adherence
iPrEx ¹	Oral Daily Truvada: 42%	51%
Partners PrEP ²	Oral Daily Truvada: 75%	81%
TDF2 ³	Oral Daily Truvada: 62%	81%
FEM-Prep ⁴	Oral Daily Truvada: No Protection	24%
VOICE ⁵	Oral Daily Truvada: No Protection	29%

Point estimates of efficacy and adherence were determined by measuring drug levels from participant samples collected at varying time points.

1. "Preexposure Chemoprophylaxis for HIV Prevention in Men Who Have Sex with Men", NEJM 2010; 363:2587-2599
2. "Antiretroviral Prophylaxis for HIV Prevention in Heterosexual Men and Women", NEJM 2012; 367:399-410
3. "Antiretroviral Preexposure Prophylaxis for Heterosexual HIV Transmission in Botswana", NEJM 2012; 367:423-434
4. "Preexposure Prophylaxis for HIV Infection among African Women", NEJM 2012; 367:411-22
5. "Understanding the Results of VOICE- Fact Sheet" Fact Sheet of the VOICE trial results

Key Principles for Prescribing PrEP

- Not offered as:
 - Sole intervention for prevention
- Prescribe as part of:
 - Comprehensive prevention plan
- Serodiscordant relationship
 - Prevent transmission
 - During attempts to conceive
- Indicated for individuals:
 - Documented HIV negative
 - Ongoing high HIV risk
- Confirmed negative test
 - As close to initiation of PrEP
- Wait to prescribe PrEP
 - Confirmed negative test

Key Principles for Prescribing PrEP

- Efficacy:
 - dependent on adherence
- Only prescribe to:
 - Those who are adherent
 - Express a willingness to do so
- Consistent condom use:
 - Critical part of a prevention plan
 - Lack of use- not a contraindication
- Contraindications:
 - Documented HIV infection
 - CrCl: <60 mL/min
 - Not ready to adhere to daily PrEP
- First prescription of PrEP:
 - Only for 30 days
 - Follow-up visit to assess:
 - Adherence, tolerance, commitment
- Next prescription of PrEP
 - 60 day prescription may be given
 - Return for 3-month testing + assess.
 - 90 days, provided patient adherent



Key Principles for Prescribing PrEP

- Require regular visits
 - At least every 3 months
 - Monitor HIV status, adherence, side effects
- Follow-up also includes:
 - Prevention services
 - Risk-reduction counseling
 - Access to condoms
 - STI screening
 - Mental health screening
 - Substance use screening
- Presenting with symptoms of acute HIV
 - HIV serologic screening test
 - Plus a plasma HIV RNA assay
- Discontinue PrEP immediately
 - Positive HIV test
 - Obtain a genotypic assay
 - Refer and link to HIV care



Truvada™ (Tenofovir + Emtriva)

- U.S. Food and Drug Administration
 - Approved for PrEP in 2012
- Taken as a once-daily oral pill
 - Same time daily
- Blocks:
 - Reverse transcriptase enzyme
- Two medicines in one:
- Emtriva
 - Emtricitabine or FTC
- Viread
 - Tenofovir disoproxil fumarate
 - TDF



<https://healthy.kaiserpermanente.org>



<http://betablog.org/fda-approves-truvada-for-prep/>

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Side Effects

Tenofovir: Treats HIV + Hepatitis B (Oral: 300 mg once daily)



New onset or worsening renal impairment

Decreases in bone mineral density

Incidence $\geq 10\%$

rash, diarrhea, headache, pain,
depression, asthenia, nausea

Emtriva: Treats HIV + Hepatitis B (Oral: 200 mg capsule once daily)



Incidence $\geq 10\%$

headache, diarrhea, nausea, fatigue, dizziness,
depression, insomnia, abnormal dreams, rash,
abdominal pain, asthenia, increased cough, rhinitis

$\geq 10\%$ in pediatric patients

Skin hyperpigmentation

Descovey™

Emtricitabine and Tenofovir Alafenamide (F/TAF)

Safety and Efficacy of Emtricitabine and Tenofovir Alafenamide (F/TAF) Fixed-Dose Combination Once Daily for Pre-Exposure Prophylaxis in Men and Transgender Women Who Have Sex With Men and Are At Risk of HIV-1 Infection

Verified July 2016 by Gilead Sciences

Sponsor:

Gilead Sciences

Estimated enrollment: 5000

Information provided by (Responsible Party):

Gilead Sciences

Study Start Date: August 2016

[ClinicalTrials.gov](https://clinicaltrials.gov) Identifier:

NCT02842086

Est. Completion Date: May 2020

First received: July 20, 2016

Last updated: NA

Last verified: July 2016

<https://clinicaltrials.gov/ct2/show/NCT02842086>

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Additional Thoughts

- When starting PrEP
 - Takes at least 7 days
 - Reach high levels of protection
- When stopping PrEP
 - Continue using PrEP for 4 weeks after last significant exposure
- PrEP does not:
 - Protect against other STIs
 - Prevent pregnancy
 - Not a cure for HIV



TIME TO PROTECTION

“The time from initiation of daily oral doses of TDF/FTC to maximal protection against HIV infection is unknown.”

There is not scientific consensus on what intracellular concentrations are protective for either drug or the protective contribution of each drug in specific body tissues...

data suggest that maximum intracellular concentrations of TFV-DP (the activated form of TDF) are reached in blood after approximately 20 days of daily oral dosing, in rectal tissue at approximately 7 days, and in cervicovaginal tissues at approximately 20 days.

No data are yet available about intracellular drug concentrations in penile tissues susceptible to HIV infection to inform considerations of protection for male insertive sex partners.”

CDC Statement on IPERGAY Trial of PrEP for HIV Prevention among MSM

Released: February 24, 2015

- Truvada™ reduced risk: among MSM by 86%
- 400 participants
- Dose of 2 pills between 2-24 hours before having sex
 - or 1 pill, if the most recent dose was taken between 1 & 6 days ago
- 2 additional single-pill doses
 - 24 and 48 hours after the last pre-sex dose
- Continue 1 pill daily if additional sex events take place
 - before the above regimen is completed

<http://www.cdc.gov/nchhstp/newsroom/2015/IPERGAY-2015-Media-Statement.html>

CDC Statement on IPERGAY Trial


Not known: If regimen will work if taken only a few hours or days before sex, without any buildup of the drug from prior use

It may take days, depending on the type of sexual exposure, for the drug to build up to an optimal level for prevention



No data: Effectiveness for heterosexual men and women and IDU or on adherence to this relatively complex PrEP regimen

“CDC continues to recommend daily dosing of PrEP and urges people at substantial risk for HIV infection and their health care providers to continue to follow current CDC guidelines.”

- https://dph.georgia.gov/sites/dph.georgia.gov/files/related_files/site_page/prEP.Letter.Fact_Sheet_2015.FINAL_WEB_JUN17.pdf
- <http://www.cdc.gov/hiv/prevention/research/prep/>
- <http://www.truvadapreprems.com/#>
- <http://www.gilead.com/responsibility/us-patient-access/truvada%20for%20prep%20medication%20assistance%20program>



PrEP Warm Line



CLINICIAN
CONSULTATION
CENTER

National rapid response for HIV management
and bloodborne pathogen exposures.

PrEPline, 855-448-7737
The CCC Pre-Exposure Prophylaxis Service
11 a.m. – 6 p.m. EST

<http://nccc.ucsf.edu/2014/09/29/introducing-the-ccc-prepline/>



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HOT OFF THE PRESS

Clinical Infectious Diseases

September 1, 2015

No New HIV Infections with Increasing Use of HIV
Preexposure Prophylaxis in a Clinical Practice Setting

Jonathan E. Volk, et. al.

HPTN 077

Cabotegravir + Rilpiverine

San Francisco

Kaiser Permanente PrEP Services

- Referrals for and initiation of PrEP since 2012
 - Increased dramatically in a large clinical practice setting
 - 657 of 1045 were started on PrEP
 - MSM (99%), Heterosexual women (3), TG-man (1)
- High rates of sexually transmitted infections
 - Among PrEP users (41% reported decreases in condom use)
 - At 6 months (30% with STI) & 12 months (50% with STI)

There were no new HIV infections in this population

Toronto Case

- Appears all aspects of care were appropriate
 - Baseline HIV test completed (HIV negative status verified)
 - Good follow up was undertaken
 - Good adherence was documented
- Reported risky condomless sex with multiple hook-up partners
 - Stated that he is “mostly a bottom”
 - Stopped using condoms: he believed “science was in my favor”
- Available information, documented resistance;
 - NRTI class: Abacavir, Tenofovir, Lamivudine, Emtricitabine
 - Integrase class: Raltegravir, Elvitegravir, Dolutegravir

What Happened to Ms. Jones?

At Ms. Jones' 1 year appointment she presented to the office alone and found to have a positive HIV confirmatory test. Labs included; CD4 675, HIV-VL 38,000, Genotype K103N, M184V. Ms. Jones states that her fiancée refused to wear condoms and took his medications on occasion.

What should be done now?

- Stop PrEP immediately
- Discuss treatment options for HIV
- Further Case Management / Support

Questions

- September 14: Access in Georgia
- September 21: Coverage and Coverage Options
- September 28: The Future of PrEP / PrEP and Me



Thank You

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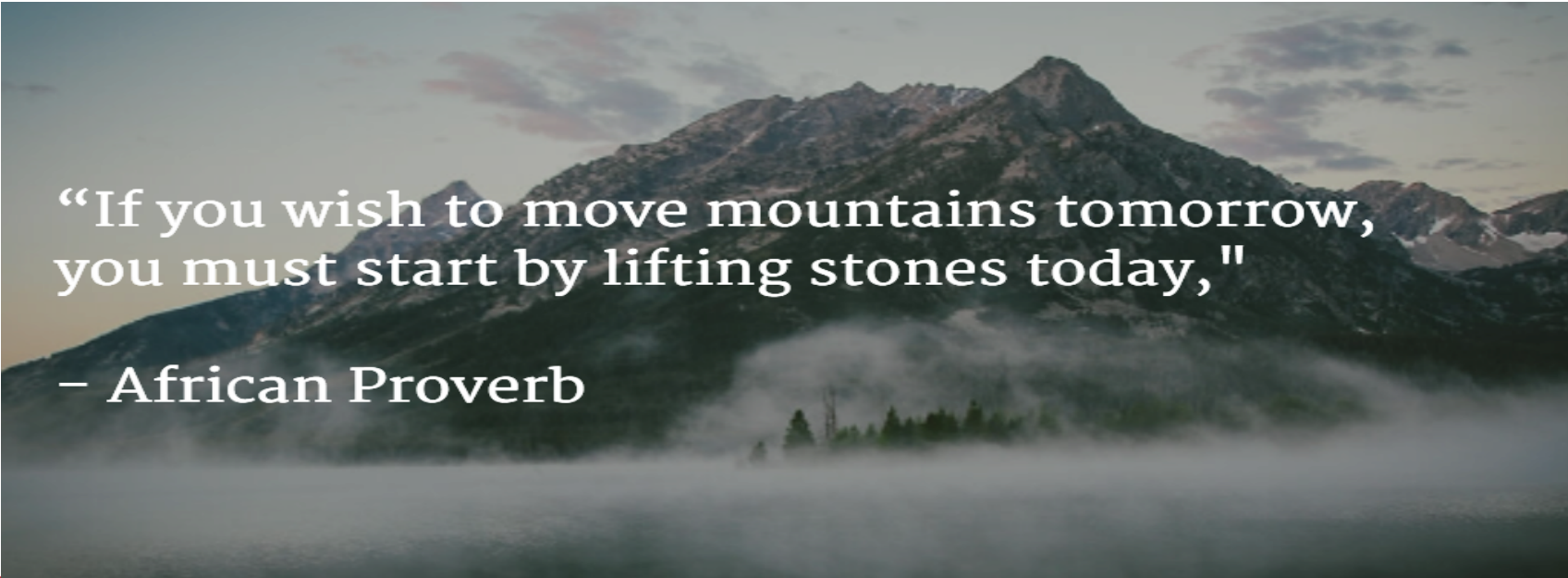
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“If you wish to move mountains tomorrow,
you must start by lifting stones today,”

– African Proverb