

# Does treating male partners of women with Bacterial Vaginosis improve cure? The STEP UP randomised controlled trial



Dr Lenka Vodstrcil  
Ms Rebecca Wigan



## Background: Bacterial Vaginosis

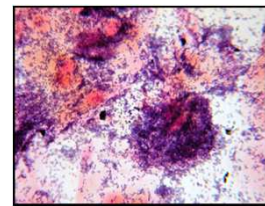
- Most common cause of vaginal dysbiosis; thin grey-white discharge & odour
- Associated with obstetric sequelae, PID, STI/HIV & impact on self-esteem, sexual relationships, and quality of life
- Pathogenesis complex: shift in the vaginal microbiota from one dominated by *Lactobacillus spp.* to one with anaerobic bacteria often with higher diversity
- Treatment with first-line antibiotics effective (~80% cure within 1 mo)
- Post-treatment recurrence is unacceptably high (>50%)
- No improvement in BV cure for decades
- Pathogenesis of recurrence is poorly understood



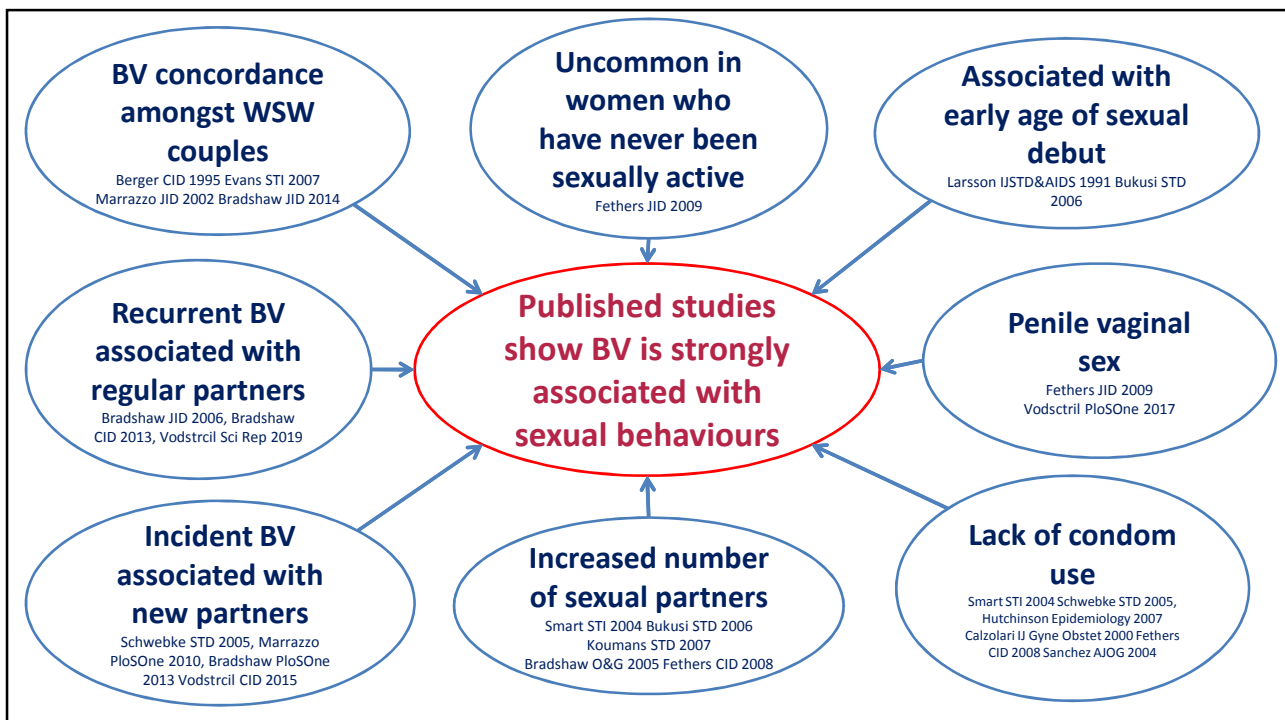
Hay 1994, Hillier 1995, Wisenfeld 2003, Atashili 2008, Cohen 2012, Bilardi 2013, Fredricks 2005, Ravel 2011, Srinivasan, 2012, Koumans 2002, <sup>0</sup>Sobel 1993, Bradshaw 2006

## Pathogenesis of post treatment recurrence

- Re-inoculation with BV-organisms from sexual partners
- Auto-inoculation from an endogenous source, or other host risk factors
- Persistence or re-emergence of BV-organisms and/or BV-biofilm
- Failure of the vagina to recolonise with desirable lactobacilli
- Is there one dominant pathway affecting all women?
- Differing mechanisms between women?
- Multifactorial?



Unemo, Bradshaw et al Lancet Infect Dis 2017

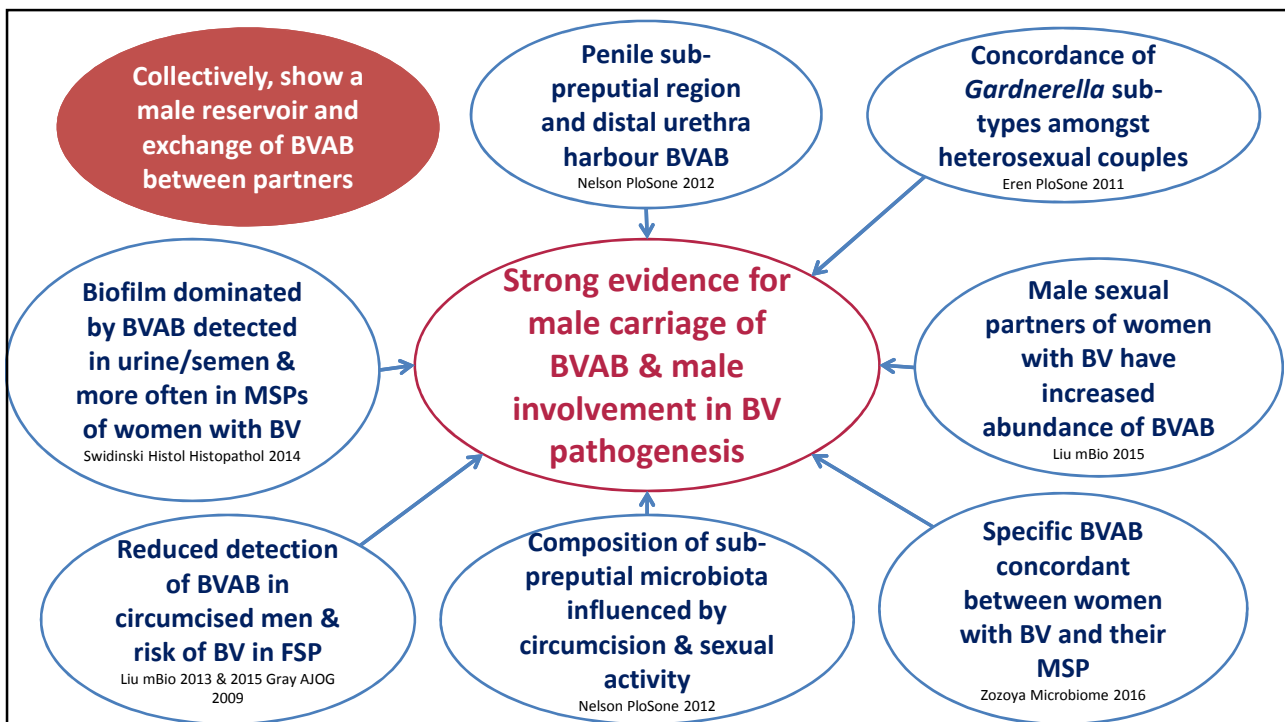


## Aetiology of BV

- Evidence that BV can be acquired through sexual activity
- But, slow progress in determining the transmitted agent(s)
- Unclear if BV is initiated by the introduction of single or multiple pathogens
  - founder organism: *Gardnerella vaginalis* or a pathogenic sub-type
  - polymicrobial consortium (“chunk of biofilm”)
  - other factors trigger overgrowth of BV-associated anaerobes/depletion of *Lactobacillus* spp.



Unemo, Bradshaw et al Lancet Infect Dis 2017, Schwabke JID 2014, Muzny Comtemp OBGYN 2018



## Evidence of a male reservoir..... But, what next?

---

- Compelling evidence for urethral & sub-preputial reservoirs for BVAB in men
- Several unanswered questions (?importance of each site, ?carriage duration, ?differences in bacteria present at each site)
- And if there are indeed aetiologic candidates present, what treatments would effectively eradicate/suppress these BVAB in men?

? Is treating male partners even possible?!?



- Despite strong evidence of male involvement in BV pathogenesis, no guidelines recommend male partner treatment

## Past male treatment trials: several limitations

---

- Only 1/6 past male partner treatment trials showed improvements
- Recent systematic review highlighted the limitations to these trials
  - Small sample sizes, randomisation methods deficient, poor retention, lack of adherence data
- Issues with therapies
  - Suboptimal, single dose therapies commonly used at that time
  - Only oral therapies evaluated in males
- Conclusions – failure of past trials was due to limitations of the trials and not evidence that BV is not sexually transmitted

*Mehta STD 2012, Muzny Contemp OBGYN 2018*



## Time for new partner treatment trials

---

- International consensus is we need rigorous partner treatment trials
- Significant challenges in ensuring successful recruitment and retention
- If reinfection is a dominant driver of recurrence it will impact on our ability to assess the efficacy of therapies directed solely to women



## Combination Therapy

---

- Dual site carriage of BVAB in men warrants evaluation of combination approaches
- In two pilot studies we have treated 50 couples and followed them to month 1
- Women with symptomatic BV ( $\geq 3$  Amsel criteria & Nugent Score  $> 3$ )
  - Oral metronidazole 400mg twice daily 7d or intravaginal 2% clindamycin cream, 7d (only if metro CI)
- Regular male partner
  - Oral metronidazole 400mg twice daily & topical clindamycin cream applied to glans penis and upper shaft (under the foreskin if uncircumcised) twice daily, 7d
- Couples collect vaginal swabs, penile skin and urine samples – weekly for one month

*Plummer PloSOne 2018*

## Pilot data

	One month n=50 couples	
	No BV recurrence N=47 (94%)	BV recurrence N=3 (6%)
<b>Past history BV</b>		
No	9(19)	0
Yes	38 (81)	3 (100)
<b>Circumcised</b>		
No	39 (83)	3 (100)
Yes	8 (17)	0 (0)
<b>UPSI on treatment</b>		
No sex/ protected sex only	39 (83)	2 (67)
Yes	8 (17)	1 (33)
<b>IUD<sup>c</sup></b>		
No	35 (74)	1 (33)
Yes	12 (26)	2 (67)
<b>Treatment adherence (female)</b>		
<70% of meds	2 (4)	0 (0)
>70% of meds	45 (96)	3 (100)
<b>Treatment adherence (male)</b>		
<70% of meds	5 (11)	0 (0)
>70% of meds	41 (89)	3 (100)

Plummer PLoSOne 2018, Erica Plummer, PhD student preliminary data 2019

## Step Up Randomised Controlled Trial

**Overall Aim:** To determine whether combined antibiotic treatment of male partners of women receiving therapy for BV improves cure rates compared to standard practice (female only treatment)

**Primary efficacy endpoint:**

- BV recurrence:  $\geq 3$  Amsel's criteria & Nugent score = 4–10, within 12 weeks of randomisation



## Randomisation groups

Females - oral metronidazole 400 mg twice daily for 7d, or if contraindicated, 7d of topical vaginal 2% clindamycin or 5 days of vaginal metronidazole gel



Males are randomised to either:

- *Intervention* – male partner treatment with dual antibiotics
  - oral metronidazole 400mg twice daily and topical 2% clindamycin cream to be applied to the glans penis and upper shaft (under the foreskin if uncircumcised) twice daily for 7d
- *Control* – current standard of care, female partner treatment only

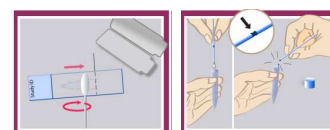


## Study procedures and methodology

- Follow up couples for 12 weeks or until BV recurrence
- Female monthly vaginal swab, smear and questionnaires:



Treatment period  
Abstain or 100% condom use



- Males baseline swab and urine & questionnaire, day 8 and endpoint:

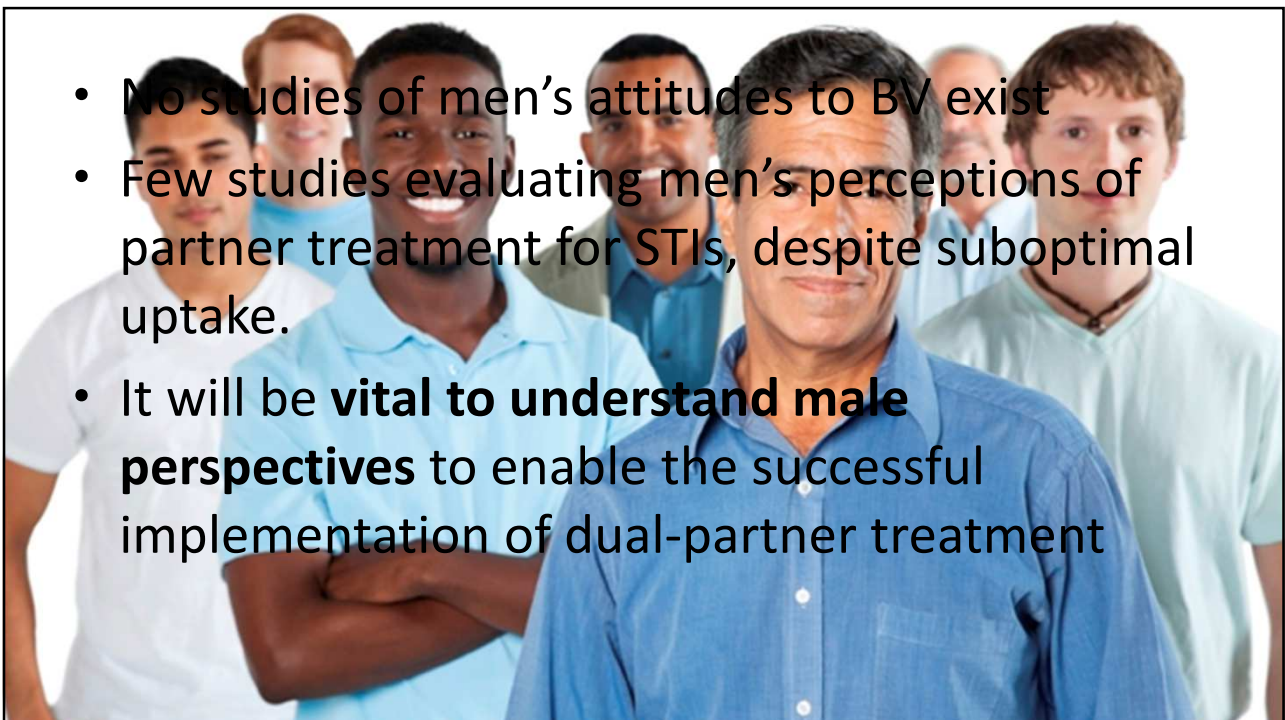
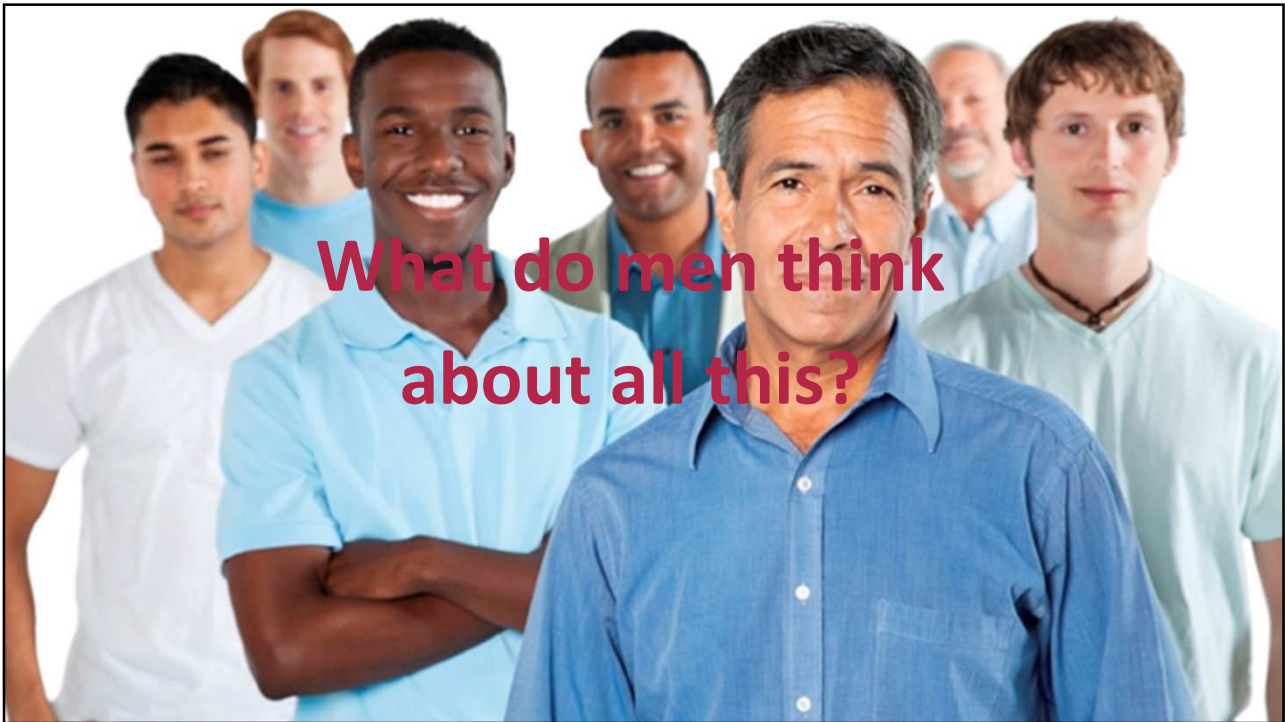


Treatment period  
Abstain or 100% condom use

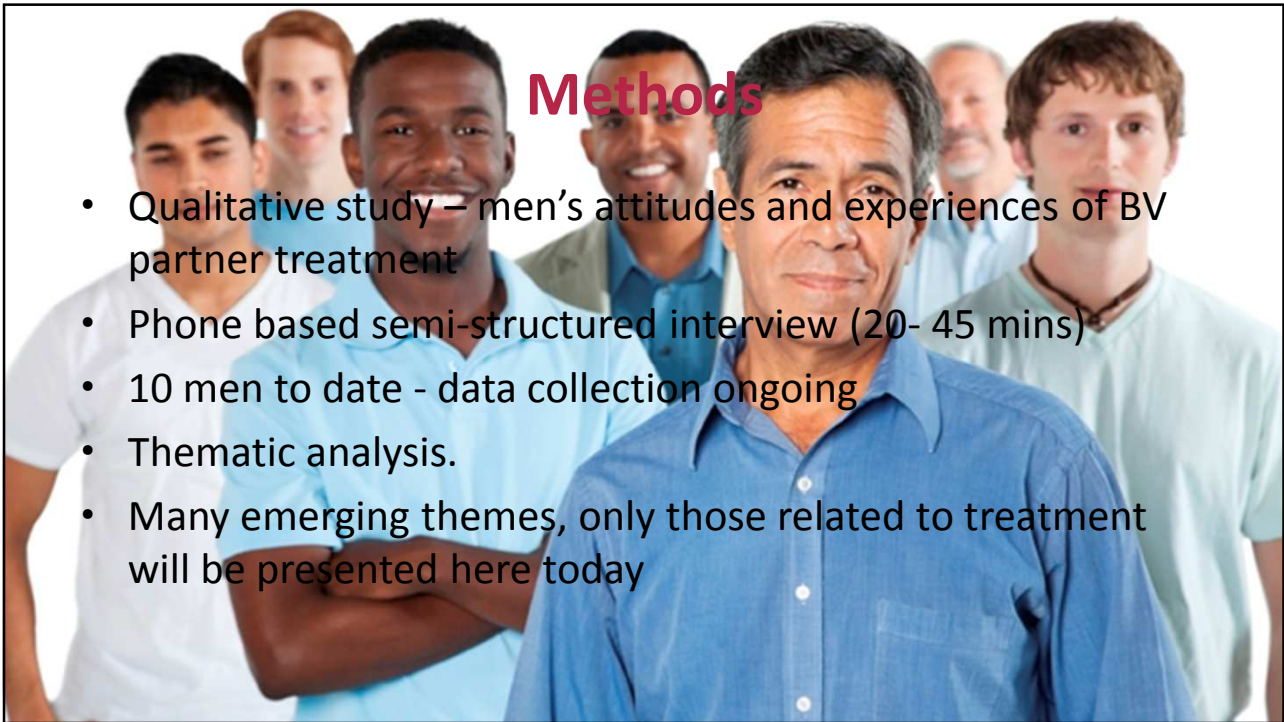
### Trial Sites

Melbourne Sexual Health Centre  
Sydney Sexual Health Centre  
Family Planning Victoria (screening)  
Family Planning NSW (screening)

**Currently Recruiting!**







## Methods

- Qualitative study – men’s attitudes and experiences of BV partner treatment
- Phone based semi-structured interview (20- 45 mins)
- 10 men to date - data collection ongoing
- Thematic analysis.
- Many emerging themes, only those related to treatment will be presented here today



## Major themes

1. Male knowledge of BV
2. Male experience of treatment
3. Motivations for accepting the study and associated treatment
4. Barriers to treatment acceptance
5. Participation experience

## 1. Knowledge of BV

- BV understood differently by different men

### Male “carriage” or BV as an STI

*“Me and my partner have kind of started thinking of it as an STI even though we have no real evidence for that...like it kind of makes sense.” –Harry*

### “Lady problem”

*“Her body isn’t doing what it should be doing. And it causes that .” - Rob*

## 2. Male experience of treatment

- **Easy**

*“Pretty easy. Go to work, don’t think about it. “ – Rob*

- **Pragmatic- Just a week**

*“It’s just a week in your life. You can give up drinking for that. It really doesn’t bother me” –David*

*“...something that you have to do.” - Rob*

- **Delay for big events**

*“... we’re just holding it off coz there was drugs, alcohol, staying up all night... we thought, we’ll hold off coz...if we’re gonna do the treatment, we’re gonna do it properly. “ - Scott*



### 3. Motivations for accepting study & treatment

---

- **Relationship**

- **Care and concern for their female partner**

- *“I’m doing this treatment and this study to support my partner, to make her feel better.” - Tristan*

- **Treatment a metaphor for the relationship**

- *“For how it affected my partner, well if I’m just gonna muck around with it, take it as a joke, I’m just taking the relationship as a joke at the same time.” - Scott*

### 3. Motivations for accepting study & treatment

---

- **Responsibility as a man and a partner**

- *“You know, as a bloke, that’s your role is to support your missus” - Tristan*

- *“I feel like in general women get the short end of the stick with basically anything to do with sex and reproduction, so anything I can do as a man that is like vaguely helpful, I feel it’s my responsibility to do” - Harry*

### 3. Motivations for accepting study & treatment

---

- **Pragmatic**

*“Well, let’s get rid of it. Or do what we can to get rid of it. Both get treated .” – Steve*

- **Self Care**

*“...you’re looking after yourself. Like, isn’t self-care one of the most important things in everyone’s life?” – Scott*

*“It’s your dick! Like ...you do the right thing by it!”- Tristan*

### 3. Motivations for accepting study & treatment

---

- **Contribute to knowledge**

*“...not just for us but for the whole community of people that might have it.” – James*

- **Seeking alternative treatments**

*“My new partner, she was trying everything, and it was really stressing her out. And so I wanted to try and help her...I guess that that was what drew me to sort of look for other avenues.” - Finn*



## 4. Barriers to treatment acceptance

---

- **I'm not the problem!** Concepts of masculinity

*"One of my best mates, he wouldn't do it, he's got too much pride... doesn't like looking weak. He likes being that strong, dominant look... [if they accept treatment] they either think that **they're getting looked at like they're the problem**. Or they don't want to see themselves as that." - Scott*

- **Avoidance**

*"Some men have that fear of the unknown. They just prefer not to know." - James*

- **No symptoms and no confirmatory test**

*"... if it's not having any physical or visible effect for their body" - David*

## 4. Barriers to treatment acceptance

---

- **Relationship**

### **Casual relationship/ not caring**

*"I think especially in casual relationships, a lot of men won't want to own up to having that and therefore won't seek treatment" - Rahul*

### **Seeing treatment as a favour**

*"I would have thought 'we're not that far into our relationship, so why do I need to do this shit for you?'..." - Rob*

## Participation experience

---

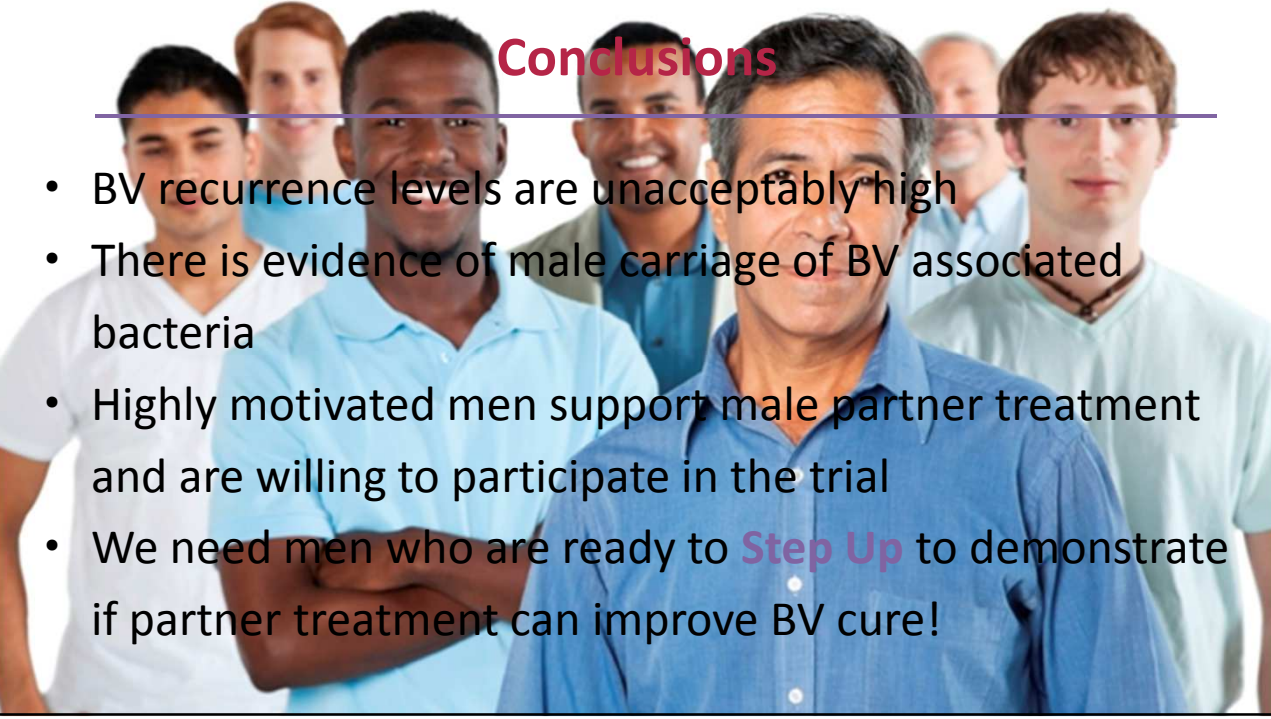
*“It’s probably just binded us closer a little bit more. And just something else that we’ve been able to tackle together and something we’ve been able to achieve. And achieve together. I guess if anything, just stronger as a couple.”*

*-James*

A photograph of a man and a woman embracing on a beach. The man is wearing a blue t-shirt and has his arms around the woman. The woman is wearing a blue top and has her arms around the man. They are both smiling and looking towards the camera. The background shows the ocean and a clear sky.

## Conclusions

---

- BV recurrence levels are unacceptably high
  - There is evidence of male carriage of BV associated bacteria
  - Highly motivated men support male partner treatment and are willing to participate in the trial
  - We need men who are ready to **Step Up** to demonstrate if partner treatment can improve BV cure!
- 
- A photograph of a group of seven men of various ethnicities and ages standing together. They are all wearing light blue or white shirts. The man in the foreground is wearing a blue button-down shirt and has his arms crossed. The other men are standing behind him, some smiling and some looking serious.

## Acknowledgements

- Project CI: A/Professor Catriona Bradshaw
- Associate investigators: Prof Christopher Fairley, Prof Jane Hocking, A/Prof Deborah Bateson, Dr Kathy McNamee, A/Prof Marcus Chen, A/Prof Eric Chow, Prof Basil Donovan, Prof Matthew Law, Dr Kathy Petoumenous, Dr Jade Bilardi
- Masters Supervisors: Dr Jade Bilardi, Dr Cathy Vaughan
- Research team: Erica Plummer, Michelle Doyle, Colette McGuinness, Marti Kaiser
- Ruthy McIver
- Funding: NHMRC Project Grant

*Study participants!*



@tayneetinsley

## Where to find out more!

- Website: [www.bvstepup.org.au](http://www.bvstepup.org.au)
- Call us: (03) 9341 6244
- Email: [stopbv@mshc.org.au](mailto:stopbv@mshc.org.au)

