## THE ROLE OF EXOGENOUS SEX STEROIDS ON THE VAGINAL MICROBIOTA: A SYSTEMATIC REVIEW

**Authors:** Ratten LK<sup>1,2</sup>, Plummer EL<sup>1,2</sup>, Bradshaw CS<sup>1,2,3</sup>, Fairley CK<sup>1,2</sup>, Garland SM<sup>4,5,6</sup>, Murray GL<sup>4,5,6</sup>, Tachedjian G<sup>7,8,9</sup>, Masson, L<sup>1,7,10,11,12</sup>, Vodstrcil LA<sup>1,2,3</sup>

<sup>1</sup>Central Clinical School, Monash University, Melbourne, Victoria

<sup>2</sup>Melbourne Sexual Health Centre, Alfred Hospital, Carlton, Victoria

<sup>3</sup>Melbourne School of Population and Global Health, The University of Melbourne, Parkville, Victoria

<sup>4</sup>Women's Centre for Infectious Diseases, The Royal Women's Hospital, Parkville, Australia

<sup>5</sup>Murdoch Children's Research Institute, Parkville, Australia

<sup>6</sup>Department of Obstetrics and Gynaecology, The University of Melbourne, Parkville, Australia

<sup>7</sup>Burnet Institute, Melbourne, Australia

<sup>8</sup>Department of Microbiology, Monash University, Clayton, Australia

<sup>9</sup>Department of Microbiology and Immunology, University of Melbourne, at the Peter Doherty Institute of Infection and Immunity, Melbourne, Australia

<sup>10</sup>Division of Medical Virology, Department of Pathology, University of Cape Town, Cape Town, South Africa

<sup>11</sup>Institute of Infectious Disease and Molecular Medicine (IDM), University of Cape Town, Cape Town, South Africa

<sup>12</sup>Centre for the AIDS Programme of Research in South Africa, Durban, South Africa

**Background:** We conducted a systematic review (PROSPERO:CRD42018107730) to determine the influence of exogenous sex steroid-use on the vaginal microbiota (VM) of reproductive-aged women using hormonal contraception (HC) and peri/post-menopausal women using hormone replacement therapy (HRT).

**Methods:** Eligible studies reported on the effect of specific HC-types or HRT-use on the VM using a molecular method. Data regarding the 'positive', 'negative' or 'neutral' effect of each HC-type and HRT-use on the VM was summarised. A HC-type/HRT-use was designated to have a positive effect if it was associated with an increased abundance of lactobacilli, a change to or maintenance of an optimal VM composition, or a decrease in bacterial diversity (specifically reflecting a low-diversity optimal VM state), relative to the control group for that study. A HC-type/HRT-use was designated as having a negative effect on the VM if it resulted in opposing effects (i.e. loss of lactobacilli, a non-optimal VM state). When no change was found, this was considered a neutral effect.

**Results:** 2647 unique studies were screened for inclusion, 266 full-texts were assessed for eligibility, and 29 studies were included in qualitative data analysis. Among 25 studies of reproductive-aged women, 15/25 reported on >1 HC type. Oestrogen-containing contraceptives, predominantly reflecting the combined-oral contraceptive pill, had a positive effect on the VM in 11/14 studies. The effect of progesterone-only contraceptives were less clear; of 22 studies, 9 showed a positive effect, 9 a negative effect, and 4 found a neutral effect. In particular, Depo-Proverause was designated as negative in 6, positive in 3, and neutral in 2 studies. All 4 studies investigating HRT-use demonstrated a positive influence of HRT-use on the VM.

**Conclusion:** Exogenous sex steroids, particularly oestrogen-containing methods, may promote an optimal VM in women. Further studies are needed to determine if specific steroid-types are more beneficial than others.

## **Disclosure of Interest Statement:**

ELP is supported by an Australian Government Research Training Program Scholarship. CKF, CSB, SMG, GT and LM are supported by Australian NHMRC Grants.