Received: 5 October 2021 | Revised: 3 January 2022 | Accepted: 5 January 2022

DOI: 10.1111/ppe.12864

Paediatric and Perinatal Epidemiology WILEY

BRIEF REPORT

Vaginal washing behaviour and fecundability among Kenyan women in a prospective preconception cohort

Erica M. Lokken[1] | Anne Pulei[2,3,4] | Brenda Oyaro[5,8] | Maureen Nyaigero[6] | Walter Jaoko[5] | Kishor Mandaliya[7] | John Kinuthia[1,6,4] | R. Scott McClelland[1,8,5,9]

[1]Department of Global Health, University of Washington, Seattle, Washington, USA

[2]Department of Human Anatomy, University of Nairobi, Nairobi, Kenya

[3]Department of Obstetrics and Gynaecology, University of Nairobi, Kenya

[4]Department of Obstetrics & Gynaecology, Kenyatta National Hospital, Nairobi, Kenya

[5]Department of Medical Microbiology, University of Nairobi, Nairobi, Kenya

[6]Research and Programs, Kenyatta National Hospital, Nairobi, Kenya

[7]Pathcare, Mombasa, Kenya

[8]Department of Medicine, University of Washington, Seattle, Washington, USA

[9]Department of Epidemiology, University of Washington, Seattle, Washington, USA

Correspondence
Erica Lokken, Department of Global Health, University of Washington, Seattle, WA, USA.
Email: elokken@uw.edu

Funding information
This work was supported by a National Institutes of Health grant (NICHD R01 HD087346-RSM). RSM received additional support for mentoring (NICHD K24 HD88229). EML was supported by a post-doctoral fellowship (NICHD F32 HD100202). Data were collected using a REDCap electronic data capture tool hosted at the University of Washington's Institute of Translational Health Science supported by grants from NCATS/NIH (UL1 TR002319). The content of this paper is solely the responsibility of the authors and does not represent the official views of the National Institutes of Health.

Abstract

Background: Intravaginal washing, practised by a significant proportion of women globally, is associated with acquisition of human immunodeficiency virus (HIV), sexually transmitted infections and bacterial vaginosis (BV). A single prior study among women in the United States found that vaginal washing was associated with lower fecundability.

Objective: To examine the association between vaginal washing and fecundability among Kenyan women.

Methods: HIV-negative Kenyan women who were trying to conceive and reported no history of infertility care-seeking were followed prospectively for incident pregnancy for up to six months. At monthly visits, participants reported the first day of last menstrual period, sexual behaviour, vaginal washing behaviour, underwent pregnancy testing and provided vaginal swabs for detection of BV by Gram stain (Nugent score ≥7). Discrete time proportional probability models were used to estimate fecundability ratio (FR) and 95% confidence interval (CI) comparing menstrual cycles when women reported vaginal washing to menstrual cycles when no vaginal washing was reported.

Results: Four hundred and fifty-eight women contributed 1,376 menstrual cycles and 255 pregnancies. At enrolment, a third (35.2%, 161 of 458) of participants reported vaginal washing with the majority using water only (73.9%, 119 of 161). After adjustment for age, frequency of unprotected intercourse and study site, vaginal washing in the prior four weeks was associated with a 29% lower fecundability (adjusted FR [aFR] 0.71, 95% CI 0.53, 0.94), which did not change after further adjustment for BV at the visit prior to each pregnancy test (aFR 0.71, 95% CI 0.54, 0.95).

Conclusions: Periconceptual vaginal washing may reduce fecundability. Potential mechanisms include vaginal washing-associated changes in the vaginal microbiota, inflammation, disruption of cervical mucus and effects on sperm function. Vaginal washing has no known health benefits, and cessation may improve women's likelihood of conceiving.

KEYWORDS
conception, fecundability, time to pregnancy, vaginal washing

1 | BACKGROUND

Intravaginal washing practices include cleansing with water or products such as vinegar, soaps or douching agents.[1] Many women globally engage in vaginal washing to improve hygiene, prevent pregnancy, prevent or treat vaginal infections, or promote sexual pleasure.[1–7] Vaginal washing is associated with increased risk of bacterial vaginosis (BV), sexually transmitted infections (STI), human immunodeficiency virus (HIV) and pelvic inflammatory disease (PID).[8–10] Only one prior study has assessed the association between vaginal douching and fecundability, finding lower fecundability among those engaging in vaginal douching.[11] Our objective was to prospectively assess the association between vaginal washing and fecundability in Kenyan women planning pregnancy.

Synopsis

Study question

Study question: Is vaginal washing associated with fecundability among Kenyan women trying to conceive?

What's already known

Intravaginal washing, practised by a significant proportion of women globally, is associated with acquisition of HIV, sexually transmitted infections and bacterial vaginosis.

What this study adds

What this study adds: Any vaginal washing in the four weeks before pregnancy testing was associated with a 29% lower per-menstrual cycle probability of pregnancy. Compared to those reporting no vaginal washing, vaginal washing with soap and water was associated with a 78% lower fecundability. Vaginal washing has no known health benefits, and cessation may improve women's likelihood of conceiving.

2 | METHODS

2.1 | Cohort selection and study procedures

Women in the Microbiota and Preterm Birth study, which enrolled women in Nairobi and Mombasa, Kenya, between 18 April 2017 and 18 March 2020, were eligible for this fecundability analysis.[12] The parent study included HIV-seronegative women who were ≤45 years old, were non-contracepting (other than condoms for STI prevention), reported a menstrual period in the prior three months (or recently discontinued hormonal contraception) and were planning to become pregnant in the next six months. Women were excluded if they were not at risk for pregnancy including having a depot medroxyprogesterone acetate (DMPA) injection within three months, were at increased risk for preterm birth (eg autoimmune diseases), used antibiotics in the last four weeks (common exclusion criterion for vaginal microbiota studies) or previously sought care for infertility. For this fecundability analysis, we excluded participants who did not contribute ≥1 menstrual cycles, those with history of PID treated in hospital, ectopic pregnancy, polycystic ovary syndrome or endometriosis and those trying to conceive for >3 menstrual cycles prior to enrolment (eFigure S1).[13,14]

At enrolment, participants completed an interview including socio-behavioural characteristics and medical history including first day of last menstrual period (LMP) and how long they had been non-contracepting and attempting pregnancy, and underwent a pelvic examination with vaginal swab collection.[12] At monthly preconception visits, participants underwent urine pregnancy testing, self-collected vaginal swabs and completed an interview reporting sexual and vaginal washing behaviour and first day of LMP. Participants were asked 'Do you use anything to clean inside your vagina?' (no/yes). If 'yes', they were asked 'In the four weeks prior to today, which of the following did you use to clean inside of your vagina?' including water only, soap and water, antiseptic, detergent, and other (specify). Most participants were eligible for up to six monthly preconception visits; those discontinuing DMPA <6 months before enrolment were eligible for up to 9 months.[15] Participants with genital symptoms were assessed and treated per Kenyan syndromic management guidelines.[16] Enrolment vaginal samples were tested for *Neisseria gonorrhoeae*, *Chlamydia trachomatis* and *Trichomonas vaginalis* (Aptima Combo-2 CT/NG Detection System, Aptima *Trichomonas vaginalis* assay; Hologic Incorporated). Directed treatment was provided for STIs detected at enrolment. Vaginal samples from all visits were assessed for BV using Nugent criteria.[17]

2.2 | Exposure

Two time-varying measures of vaginal washing were considered: (1) any vaginal washing in the last four weeks (no/yes) and (2) type of vaginal washing in the last four weeks (none, water only, soap and water). Two cycles were characterised by antiseptic use and were included with soap and water. Three cycles with an 'other' type of vaginal washing were included with either water only or soap and water based on review of the substances specified.

2.3 | Outcome

For each participant, number of menstrual cycles to first incident pregnancy was calculated using reported first days of LMPs and monthly urine pregnancy test results.[13] In July 2018, a question was added to the monthly interview for report of additional first days of LMPs ('interim menstrual cycles') for women who missed preconception visits (n = 82 cycles reported). One-hundred and thirty participants had visits prior to July 2018, and in these cases, 'interim menstrual cycles' were derived (n = 41 cycles), as previously described.[13] Participants were censored during follow-up for

biomedical infertility treatment ($n = 3$), not conceiving during follow-up ($n = 73$), withdrawal or loss to follow-up ($n = 49$) and at the onset of the COVID-19 pandemic ($n = 35$).

2.4 | Statistical analysis

We used discrete time proportional probability models to generate fecundability ratios (FR) and 95% confidence intervals (95% CI) estimating the association between vaginal washing and fecundability.[14,18] For participants with prior conception attempt time, we utilised delayed entry to enter participants into the analysis at their current menstrual cycle of trying to reduce left truncation bias. Based on existing literature, knowledge of the study population and consideration of causal relationships, maternal age (years: <25, 25–29, 30–34, 35–39, 40–45), frequency of unprotected intercourse in the prior four weeks (none, 1–4, 5–8, ≥9) and study site were included *a priori* in multivariable models.[1,19] In a second adjusted model, we included BV (Nugent score ≥7) at the visit prior, as women may have engaged in vaginal washing because of BV.[13]

2.4.1 | Missing data

For 123 derived or reported 'interim menstrual cycles' (8.9% of cycles) and for rare data missingness for attended visits (0.03% of cycles), missing vaginal washing and unprotected intercourse data were imputed using data from the last visit carried forward.

2.4.2 | Sensitivity analyses

First, we excluded those with potential sub-fecundity (*N. gonorrhoeae*, *C. trachomatis*, *T. vaginalis* or PID at enrolment, any history of PID diagnosis or treatment for *N. gonorrhoeae*, *C. trachomatis*, *T. vaginalis* or syphilis; self-report of fibroids or unknown uterine abnormality; DMPA use within six months of enrolment, HIV-seropositive partner). Second, we excluded derived and reported menstrual cycles. Third, we included women reporting ≤6 menstrual cycles of pre-enrolment conception attempt time.

2.4.3 | Ethics approval

The Kenyatta National Hospital-University of Nairobi and University of Washington ethics committees approved this study. Participants provided written informed consent.

3 | RESULTS

The 458 participants were a median of 29 years old (IQR 25–34), and most reported no prior conception attempt time (80.1%, $n = 367$) (Table 1). There were 255 pregnancies across 1,376 menstrual cycles. Twenty-six per cent (359 of 1376) of cycles were exposed to vaginal washing (Table 2), with water accounting for 20.9% (287 of 1376) of cycles and soap and water 5.2% (42 of 1376) of cycles. After adjustment for age, frequency of unprotected intercourse and study site, vaginal washing in the prior four weeks was associated with a 29% lower fecundability (adjusted FR (aFR) 0.71, 95% CI 0.53,0.94), which was similar after further adjustment for BV (aFR 0.71, 95% CI 0.54, 0.95) (Table 2). Compared to no vaginal washing, vaginal washing with water only was associated with a 17% lower fecundability (aFR 0.83, 95% CI 0.62, 1.10) and vaginal washing with soap and water was associated with a 78% lower fecundability (aFR 0.22, 95% CI 0.07, 0.71). Results were similar for sensitivity analyses excluding women with potential sub-fecundity, excluding derived and reported cycles and including participants with up to 6 cycles of pre-enrolment conception attempt time (eTable S1).

4 | COMMENT

4.1 | Principal findings

Among Kenyan women, recent vaginal washing was associated with a 29% lower per-menstrual cycle probability of pregnancy. Compared to those reporting no vaginal washing, vaginal washing with soap and water was associated with a 78% lower fecundability.

4.2 | Strengths of the study

Strengths include the prospective design, monthly ascertainment of vaginal washing and inclusion of the first menstrual cycle at risk for pregnancy for most participants.

4.3 | Limitations of the data

First, data on frequency, timing in relation to intercourse and reasons for vaginal washing were not collected, so we were unable to assess these characteristics. Second, sexual frequency was not collected for a biologically confirmed fertile window, which may contribute to residual confounding. Lastly, we were unable to assess mediation of the association between vaginal washing and fecundability by the vaginal microbiota.

4.4 | Interpretation

Our results are similar to the only other study of vaginal washing and fecundability we are aware of.[11] In a retrospective cohort study of vaginal douching among 840 women in King County, WA, vaginal douching >2 times/year prior to pregnancy was associated with a 31% lower fecundability compared to never/rare vaginal douching.

Vaginal washing may reduce the presence or concentration of optimal *Lactobacillus* species and promote ascension of BV-associated

TABLE 1 Enrolment characteristics for 458 Kenyan women trying to conceive

Characteristic	Total *N* = 458
Demographics	
Age (years)	
<25	87 (19.0)
25–29	147 (32.1)
30–34	121 (26.4)
35–39	84 (18.3)
40–45	19 (4.2)
Education (years)	
<8	29 (6.3)
8–11	137 (29.9)
12–15	207 (45.2)
≥16	85 (18.6)
Monthly Household Income (KSh)[a]	
<2500	13 (2.9)
2500–10,000	136 (29.9)
10,000–30,000	197 (43.3)
30,000–75,000	70 (15.4)
>75,000	39 (8.6)
Married or living with partner	439 (95.9)
Partner's HIV-serostatus[b]	
HIV-seronegative	345 (75.7)
HIV-seropositive	22 (4.8)
Unknown	89 (19.5)
Reproductive History	
Most recent contraceptive method[c]	
None	102 (22.3)
Condoms	24 (5.2)
OCP	10 (2.2)
DMPA Injectable	18 (3.9)
Copper IUD	127 (27.7)
Implant	175 (38.2)
Other	2 (0.4)
Ever pregnant	430 (93.9)
Number of menstrual cycles of prior conception attempt time[d]	
0	367 (80.1)
1	59 (13.0)
2	19 (4.2)
3	13 (2.8)
Abnormal uterus (fibroids or other/unknown pathology)[e]	8 (1.3)
Sexual behaviour and vaginal washing in last 4 weeks	
Any vaginal washing	161 (35.2)
Type of vaginal washing	
None	297 (64.9)
Water only	119 (26.0)
Soap + Water	42 (9.2)
Antiseptics	0 (0.0)
Frequency of unprotected intercourse[f]	
No unprotected intercourse	43 (9.4)
1–4	152 (33.3)
5–8	115 (25.2)
≥9	147 (32.2)
STI and BV[g]	
History of PID with outpatient treatment	1 (0.2)
History of STI[h]	6 (1.3)
N. gonorrhoeae	3 (0.7)
C. trachomatis	34 (7.5)
T. vaginalis	4 (0.9)
BV (Nugent ≥7)	164 (35.8)

Abbreviations: BV, Bacterial vaginosis; DMPA, Depo medroxyprogesterone acetate; IUD, Intrauterine device; KSh, Kenyan shillings; OCP, Oral contraceptive pills; PID, Pelvic inflammatory disease; STI, Sexually transmitted infection.

[a]*N* = 455.

[b]*N* = 456.

[c]Participants reporting OCP, contraceptive implant, or copper IUD discontinuation >2 months prior to enrollment or a last DMPA injection >6 months prior to enrollment were classified as 'none' for this analysis.

[d]Women reporting >3 cycles of conception attempt time prior to enrollment were excluded for this analysis.

[e]Self-reported.

[f]*N* = 457.

[g]STI results were missing for *N* = 4 for *N. gonorrhoeae*, *N* = 4 for *C. trachomatis*, and *N* = 5 for *T. vaginalis*.

[h]Self-reported history of syphilis, chlamydia, gonorrhea, and/or trichomoniasis.

bacteria to the upper reproductive tract causing sub-clinical or clinical PID.[7,8,20–22] There could also be an inflammatory response to vaginal washing independent of microbiota, as well as effects on cervical mucus.

Whether associations between vaginal washing and adverse reproductive outcomes are causal versus due to a BV episode that precipitated the vaginal washing is debated.[9,23,24] We previously reported associations between recent and persistent BV and lower fecundability in this cohort.[13] Our current analysis assessing vaginal washing had similar results in adjusted models with or without BV. Due to the timing of sample collection visits and monthly assessment of vaginal washing behaviour, we are unable to employ marginal structural models to assess mediation of the association between vaginal washing and lower fecundability by BV. A study addressing this question would need to measure both vaginal washing and BV at more than one point during each menstrual cycle.

5 | CONCLUSIONS

Among Kenyan women attempting pregnancy, there was an association between recent vaginal washing and lower

TABLE 2 Unadjusted and adjusted association between vaginal washing and fecundability among 458 Kenyan women trying to conceive

	Menstrual Cycles Exposed (*N* = 1376)	PregnanciesExposed (*N* = 255)	Unadjusted FR	Model 1: Adjusted FR[a]	Model 2: Adjusted FR[b]
Exposure	***n*(%)**	***n*(%)**	**(95% CI)**	**(95% CI)**	**(95% CI)**
Primary Analysis					
Any vaginal washing in last 4 weeks					
No	1017 (73.9)	204 (80.0)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Yes	359 (26.1)	51 (20.0)	0.72 (0.54, 0.96)	0.71 (0.53, 0.94)	0.71 (0.54, 0.95)
Secondary Analysis					
Type of vaginal washing in last 4 weeks					
None	1017 (73.9)	204 (80.0)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Water only	287 (20.9)	48 (18.8)	0.85 (0.63, 1.13)	0.83 (0.62, 1.10)	0.83 (0.62, 1.11)
Soap and water[c]	72 (5.2)	3 (1.2)	0.21 (0.07, 0.67)	0.22 (0.07, 0.71)	0.23 (0.07, 0.71)

[a]Maternal age, study site, and frequency of unprotected intercourse were included in Model #1.

[b]Maternal age, study site, frequency of unprotected intercourse, and BV at the visit prior (time-varying) were included in Model #2.

[c]Includes n=2 cycles with report of antiseptic use.

fecundability that was strongest among those using soap and water. Vaginal washing cessation may improve women's likelihood of conceiving.

ACKNOWLEDGEMENTS

We thank the study staff in Nairobi, Mombasa and Seattle for their commitment, creativity and teamwork. We are also grateful to Kenyatta National Hospital, Coast General Teaching and Referral Hospital, and the Mombasa County Department of Health for supporting this research and providing clinical and laboratory space. Lastly, we are deeply appreciative of the participants' dedication to this study.

AUTHOR CONTRIBUTIONS

RSM is the principal investigator of the parent study, supervising study protocol development and implementation. JK and WJ served as site principal investigators, overseeing study staff and implementation at Kenyatta National Hospital and Ganjoni Health Center. RSM, EML, AP, BO, JK, WJ, and KM participated in designing and implementing the parent study, protocol, data collection tools, and staff training. WJ and KM oversaw laboratory methods. EML, AP, and RSM designed this secondary analysis. EML directed the study, conducted the statistical analyses, and wrote the first draft of the manuscript. All authors reviewed and approved the final manuscript.

CONFLICT OF INTEREST

RSM receives research funding, paid to the University of Washington, from Hologic Incorporated.

PRESENTATION INFORMATION

This research was presented as an oral presentation at the STI & HIV 2021 World Congress held virtually on 14–17 July 2021.

DATA AVAILABILITY STATEMENT

This study was conducted with approval from the Kenyatta National Hospital - University of Nairobi Ethics and Research Committee (KNH-UON ERC), which requires that we release data from Kenyan studies (including de-identified data) only after they have provided their written approval for additional analyses. As such, data for this study will be available from the authors upon request, with written approval for the proposed analysis from the KNH/UON ERC. To request these data, please contact KRTC Administrator at kenyares@uw.edu.

ORCID

Erica M. Lokken https://orcid.org/0000-0002-3285-4751

REFERENCES

1. Nsereko E, Moreland PJ, Dunlop AL, Nzayirambaho M, Corwin EJ. Consideration of cultural practices when characterizing the vaginal microbiota among African and African American women. *Biol Res Nurs*. 2021;23:91-99.
2. Masese L, McClelland RS, Gitau R, et al. A pilot study of the feasibility of a vaginal washing cessation intervention among Kenyan female sex workers. *Sex Transm Infect*. 2013;89:217-222.
3. Hull T, Hilber AM, Chersich MF, et al. Prevalence, motivations, and adverse effects of vaginal practices in Africa and Asia: findings from a multicountry household survey. *J Women's Health*. 2011;20:1097-1109.
4. Kinuthia J, Richardson BA, Drake AL, et al. Sexual behavior and vaginal practices during pregnancy and postpartum: implications for HIV prevention strategies. *J Acquir Immune Defic Syndr*. 2017;74:142-149.
5. Crann SE, Cunningham S, Albert A, Money DM, O'Doherty KC. Vaginal health and hygiene practices and product use in Canada: a national cross-sectional survey. *BMC Women's Health*. 2018;18:1-8.
6. United States National Center for Health Statistics. Key statistics from the national survey of family growth - d listing: douching, vaginal. https://www.cdc.gov/nchs/nsfg/key_statistics/d.htm#douching. (last Accessed June 2021).

7. Lokken EM, Manguro GO, Abdallah A, et al. Association between vaginal washing and detection of Lactobacillus by culture and quantitative PCR in HIV-seronegative Kenyan women: a cross-sectional analysis. *Sex Transm Infect*. 2019;95:455-461.
8. Ness RB, Hillier SL, Richter HE, et al. Douching in relation to bacterial vaginosis, lactobacilli, and facultative bacteria in the vagina. *Obstet Gynecol*. 2002;100:765-772.
9. Low N, Chersich MF, Schmidlin K, et al. Intravaginal practices, bacterial vaginosis, and HIV infection in women: individual participant data meta-analysis. *PLoS Med*. 2011;8:e1000416.
10. Scholes D, Daling J, Stergachis A, Weiss N, Wang S, Grayston J. Vaginal douching as a risk factor for acute pelvic inflammatory disease. *Obstet Gynecol*. 1993;601-606.
11. Baird DD, Weinberg CR, Voigt LF, Daling JR. Vaginal douching and reduced fertility. *Am J Public Health*. 1996;86:844-850.
12. Lokken EM, Mandaliya K, Srinivasan S, et al. Impact of preconception vaginal microbiota on women's risk of spontaneous preterm birth: protocol for cohort study a prospective case-cohort study. *BMJ Open*. 2020;10:e035186.
13. Lokken EM, Manhart LE, Kinuthia J, et al. Association between bacterial vaginosis and fecundability in Kenyan women planning pregnancies: a prospective preconception cohort study. *Hum Reprod*. 2021;36:1279-1287.
14. Weinberg CR, Baird DD, Wilcox AJ. Sources of bias in studies of time to pregnancy. *Stat Med*. 1994;13:671-681.
15. Yland JJ, Bresnick KA, Hatch EE, et al. Pregravid contraceptive use and fecundability: prospective cohort study. *Hum Reprod*. 2020;371:m3966.
16. National AIDS & STI Control Programme of Kenya. *Kenya National Guidelines for Prevention*. Management and Control of Sexually Transmitted Infections; 2018.
17. Nugent RP, Krohn MA, Hillier SL. Reliability of diagnosing bacterial vaginosis is improved by a standardized method of Gram stain interpretation. *J Clin Microbiol*. 1991;29:297-301.
18. Weinberg C, Wilcox A, Baird DD. Reduced fecundability in women with prenatal exposure to cigarette smoking. *Am J Epidemiol*. 1989;129:1072-1078.
19. Wesselink AK, Rothman KJ, Hatch EE, Mikkelsen EM, Sorensen HT, Wise LA. Age and fecundability in a North American preconception cohort study. *Am J Obstet Gynecol*. 2017;217(667):667.
20. Beigi RH, Wiesenfeld HC, Hillier SL, Straw T, Krohn MA. Factors associated with absence of H2O2-producing Lactobacillus among women with bacterial vaginosis. *J Infect Dis*. 2005;191:924-929.
21. Haggerty CL, Totten PA, Tang G, et al. Identification of novel microbes associated with pelvic inflammatory disease and infertility. *Sex Transm Infect*. 2016;92:441-446.
22. Taylor BD, Darville T, Haggerty CL. Does bacterial vaginosis cause pelvic inflammatory disease? *Sex Transm Dis*. 2013;40:117-122.
23. Brotman RM, Klebanoff MA, Nansel TR, et al. A longitudinal study of vaginal douching and bacterial vaginosis - a marginal structural modeling analysis. *Am J Epidemiol*. 2008;168:188-196.
24. Gondwe T, Ness R, Totten PA, et al. Novel bacterial vaginosis-associated organisms mediate the relationship between vaginal douching and pelvic inflammatory disease. *Sex Transm Infect*. 2020;96:439-444.

SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

How to cite this article: Lokken EM, Pulei A, Oyaro B, et al. Vaginal washing behaviour and fecundability among Kenyan women in a prospective preconception cohort. *Paediatr Perinat Epidemiol*. 2022;36:205–210. doi:10.1111/ppe.12864