NCT 03536923

Use of Leva Incontinence System in Treating Bladder Incontinence

May 14, 2017

Project No.: NESCA-Renovia-01
Sponsor No: POC Trial LV-001 UI

AN OPEN-LABEL STUDY TO ASSESS THE EFFECTIVENESS OF THE *LEVA* INCONTINENCE SYSTEM IN TREATING BLADER INCONTINENCE

FDA Statement

leva Incontinence System ™ is an FDA-approved Class II medical device. As such it has been tested and found to conform with the requirements of IEC 60601-1:2005 (3RD Edition), Medical Electrical Equipment-Part 1: General requirements for basic safety and essential performance; IEC 60601-1-2:2007, Medical electrical equipment-Part1-2:General requirements for basic safety and essential performance-Collateral standard: Electromagnetic compatibility-Requirements and tests; and IEC 60601-1-1-11, General requirements for basic safety and essential performance-Collateral standard: Requirements for medical electrical equipment and medical electrical systems used in the home healthcare environment. The results of these tests indicate that the device is safe for its intended use. In addition, a biocompatibility evaluation was performed to satisfy ISO 10993-1 and FDA requirements. All patient contacting materials have been tested, and passed cytotoxicity, sensitization and irritation or intra-cutaneous standards. *leva* poses little to no risk to the patient if used as instructed.

GCP Statement

This study is to be performed in full compliance with the protocol, Good Clinical Practices (GCP), and applicable regulatory requirements. All required study documentation will be archived as required by regulatory authorities.

Confidentiality Statement

Protocol Version 2.0
May 5, 2017

1 PROTOCOL REVISION HISTORY

Date/Name	Description
17 Feb 2017	Version 1.0
05 May 2017	Version 2.0

PRINCIPAL INVESTIGATOR AND SPONSOR – SIGNATORIES

AN OPEN-LABEL STUDY TO ASSESS THE EFFECTIVENESS OF THE *LEVA* INCONTINENCE SYSTEM IN TREATING BLADER INCONTINENCE

SPONSOR:

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AN OPEN-LABEL STUDY TO ASSESS THE EFFECTIVENESS OF THE *LEVA* INCONTINENCE SYSTEM IN TREATING BLADER INCONTINENCE

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3 SYNOPSIS

Device:	*leva* Incontinence System™
Clinical Indication:	Urinary Incontinence
Study Objective:	The objective of this study is to assess the effectiveness of the *leva* Incontinence System™ in treating bladder incontinence.
Summary of Study Design:	An open-label study. Screening of subjects will occur over 1-2 study visits to determine study eligibility. Up to 25 subjects meeting inclusion/exclusion criteria at Screening will complete about 6-8 weeks of training and testing with a device to improve the strength of their pelvic floor muscles. Weekly during the study the subjects will complete tests using the *leva* device to assess changes in their pelvic floor muscle strength. Subjects will also complete surveys to assess improvements in the symptoms of their urinary incontinence. The FSFI and PISQ-IR surveys will be provided to subjects to complete at the Screening visit and upon study completion and will be returned in a sealed envelope for review after conduct is completed. Completion of the FSFI and PISQ-IR surveys is optional. Subjects that complete the study will be asked to participate in an optional post study interview with the Study Director and a marketing professional to better understand the subjects' experience using the device. The interview is optional.
Blinding:	Unblinded
Number of Subjects:	Up to 25 subjects meeting inclusion/exclusion criteria at Screening visit will return to the clinic to participate in the treatment phase of the study.
Study Treatment:	*leva* Incontinence System™

Key Assessments:	The following analyses will be performed:
	Efficacy:
	• *leva* device angle measurements
	• Survey evaluations of incontinence including:
	  ○ Urinary Incontinence Distress Inventory (UDI-6)
	  ○ Incontinence Impact Questionnaire (IIQ-7)

	○ Patient's Global Impression of Severity (PGI-S) ○ Revised Urinary Incontinence Scale (RUIS) ○ Patient's Global Impression of Improvement (PGI-I) ○ Clinician's Global Impression of Improvement (CGI-I) ○ Voiding diary **Safety and Tolerability:** ○ Subjects will be monitored for adverse events and serious adverse events.

4 STUDY EVENTS FLOW CHART

Study Procedures	Screen	Training Visits	Week 3	Week 6 Visit	End of Study/Early Termination
Visit →	1**	2-30	11	26	31
Inclusion/Exclusion Criteria	X				
Informed Consent	X				
Demographic data	X				
Medical History	X				
Height/Weight	X				
Urine Pregnancy Test	X				
Oral alcohol/Urine Drug Screen	X				
AE Monitoring		X	X	X	X
Concomitant Medication	X	X	X	X	X
Survey: MESA	X				
Surveys: UDI-6, IIQ-7, PGI-S, RUIS	X	X weekly	X	X	X
Surveys: FSFI, PISQ-IR (optional)	X				X
Patient's & Clinical Global Impression-Improvement			X	X	X
Voiding Dairy	X		X		X
leva Training	X	X	X	X	
leva Testing/Angle Measurements	X	X* visits 6, 16 & 21	X*	X*	X*
Interview subject about experience using the device (optional)					X

*Preferably on Mondays ** Screening activities can be conducted over 1-2 visits

5 ABBREVIATIONS

AE	Adverse event
CFR	Code of Federal Regulations
CGI-I	Clinical Global Impression of Improvement
CRF	Case Report Form
CRU	Clinical Research Unit
EOS	End of Study
FDA	Food and Drug Administration
FSFI	Female Sexual Function Index
GCP	Good Clinical Practice
ICF	Informed Consent Form
ICH	International Conference on Harmonisation
IIQ-7	Incontinence Impact Questionnaire
IRB	Institutional Review Board
MESA	Medical, Epidemiologic and Social Aspects of Aging
N	Number of subjects
PGI-I	Patient's Global Impression of Improvement
PGI-S	Patient's Global Impression of Severity
PI	Principal Investigator
PISQ-IR	Pelvic Organ Prolapse/Incontinence Sexual Questionnaire
QA	Quality Assurance
RUIS	Revised Urinary Incontinence Scale
SAE	Serious adverse event
SAP	Statistical analysis plan
SD	Standard deviation
UAE	Unexpected adverse event
UDI-6	Urinary Incontinence Distress Inventory
US	United States

6 BACKGROUND

Injury or weakening of the pelvic floor muscles can lead to pelvic floor disorders including urinary incontinence, pelvic organ prolapse, fecal incontinence or sexual dysfunction. These conditions affect 1 in 4 women of all ages and can make a significant impact on quality of life. Pelvic Floor Muscle Exercises, also known as Kegel's, are the first-line conservative treatment for pelvic floor disorders and specifically for urinary incontinence. Studies have shown that performing pelvic floor muscle exercises and/or pelvic floor physical therapy is the most effective non-invasive treatment for urinary incontinence. Pelvic Floor Muscle Therapy is advocated as the first-line of treatment for urinary incontinence by the American College of Obstetrics and Gynecology, the American Urogynecological Society, the Agency for Healthcare Research and Quality.

Pelvic Floor Muscle Exercises was first described by Arnold Kegel almost 60 years ago. Most women have trouble identifying and contracting the correct muscles when performing these exercises. The novel device that is an intravaginal system, *Ieva* Incontinence System ™ allows women to have real-time visual verification that the exercises are performed correctly and consistently. I*eva* Incontinence System™ also measures and records the results of every session performed while using the device thus assuring patient compliance. In the proposed study we aim to clinically show improvement of incontinence symptoms with use of *Ieva* Incontinence System™ for performing Pelvic Floor Muscle Exercises.

The association between urinary incontinence and female sexual dysfunction has been described in the literature. The relationship is reported by Salonia et al (2004) however, overall there is a paucity of research in this area. We will evaluate if women who show improvement in incontinence symptoms with the use of the *Ieva* Incontinence System™ and who complete the optional FSFI and PISQ-IR surveys have changes in their responses to the survey questions and will then determine if further research is warranted.

7 STUDY OBJECTIVE AND ENDPOINT

7.1 Study Objective

The objective of this study is to assess the effect of the *Ieva* device on signs and symptoms of urinary incontinence as measured by the endpoints descried below.

7.2 Study Endpoint(s)

Efficacy:

1. *Ieva* device angle measurements
2. Survey evaluations of incontinence including:
    a. Urinary Incontinence Distress Inventory (UDI-6)
    b. Incontinence Impact Questionnaire (IIQ-7)
    c. Patient's Global Impression of Severity (PGI-S)
    d. Revised Urinary Incontinence Scale (RUIS)
    e. Patient's Global Impression of Improvement (PGI-I)
    f. Clinician's Global Impression of Improvement (CGI-I)
    g. Voiding diary

Safety and Tolerability:

1. Reported Adverse Events (AEs) and Serious Adverse Events (SAEs)

8 INVESTIGATIONAL PLAN

8.1 Overall Study Design and Plan

An open-label study in adult women with urinary incontinence.

Screening of subjects will occur in one to two visits to determine study eligibility.

Up to 25 subjects meeting inclusion/exclusion criteria at screening will participate in 6 (up to 8 weeks) of twice daily training sessions using the *Ieva* device. Subjects will be allowed up to 8 weeks to complete the study to accommodate scheduling issues, menstrual periods or planned vacations.

Training sessions last 2.5 minutes with alternating 15 seconds of voluntary contraction of the pelvic floor muscles and 15 seconds of rest.

Changes in urinary incontinence will be assessed by symptoms of incontinence, *Ieva* angle measurements and patient's and clinician's assessment of global improvement over the study period.

All subjects enrolled in the study will be asked to complete the FSFI and PISQ-IR surveys upon enrollment and at study end. Completion of the FSFI and PISQ-IR is optional, and completed surveys will be returned in a sealed envelope and reviewed following study completion.

All subjects who complete this study will be invited to participate in an optional interview with the Study Director and a marketing professional to better understand their experiences using the device. The interview will last up to one hour at the final visit.

8.1.1 Confinement and Return Visits

The screening visit may take up to 1 hour and the return visits will last about 15 minutes. See Study Events Flow Chart (Section 4).

For each visit, the subjects will report to the clinic at the time indicated by the Clinical Research Unit (CRU) and remain confined until completion of the training/testing with the female *Ieva* Trainer who is a licensed healthcare professional.

At the discretion of study staff, a female *Ieva* Trainer therapist may be sent to a subject's home for training/testing. There will be no additional charge for an at-home visit.

There are no overnight stays required for this study. At all times, a subject may be required to remain at the CRU for longer at the discretion of the Principal Investigator (PI).

8.2 Risks and/or Benefits to Subjects

Ieva Incontinence System ™ is an FDA-approved Class II medical device. As such it has been tested and found to conform with the requirements of IEC 60601-1:2005 (3RD Edition), Medical Electrical Equipment-Part 1: General requirements for basic safety and essential performance; IEC 60601-1-2:2007, Medical electrical equipment-Part1-2:General requirements for basic safety and essential performance-Collateral standard: Electromagnetic compatibility-Requirements and tests; and IEC 60601-1-1-11, General requirements for basic safety and essential performance-Collateral standard: Requirements

for medical electrical equipment and medical electrical systems used in the home healthcare environment. The results of these tests indicate that the device is safe for its intended use. In addition, a biocompatibility evaluation was performed to satisfy ISO 10993-1 and FDA requirements. All patient contacting materials have been tested, and passed cytotoxicity, sensitization and irritation or intra-cutaneous standards. *Ieva* poses little to no risk to the patient if used as instructed.

The risks of use of the *Ieva* device are minimal to none however, there may be some unknown or infrequent or unforeseeable risks associated with the use of the device. The potential risks may include embarrassment with use of the intravaginal device; however the use of this should not conceptually differ from use of a tampon. Risks of course will be monitored throughout the entirety of the study.

8.3 Selection of Study Population

8.3.1 Inclusion Criteria

Subjects must fulfill all of the following inclusion criteria to be eligible for participation in the study, unless otherwise specified:

1. Subjects must be female.
2. Subjects must be capable of giving informed consent.
3. Subjects should be between at least 18 years of age.
4. Subjects must have a diagnosis of or symptoms of predominant mild to moderate urinary incontinence based on the results of the completed urinary incontinence surveys.

8.3.2 Exclusion Criteria

Subjects must not be enrolled in the study if they meet any of the following criteria:

1. Absence of a vagina.
2. Positive drug or alcohol test at the Screening visit.
3. Post-menopausal defined as absence of a period for over 12 months.
4. Pregnancy or being less than 12 months post-partum.
5. Greater than 3 vaginal deliveries or prior operative delivery (e.g. use of vacuum, forceps or abdominal pressure).
6. Symptoms of stage II or greater pelvic organ prolapse.
7. BMI >31 kg/m2.
8. Diagnosis of any neurological disorder.
9. Prior lower back or pelvic surgery, including prior surgery for SUI.

10. Prior pelvic radiation.

11. Current or recurrent vaginal infections (>3 per year).

12. Painful bladder syndrome, active or chronic pelvic pain.

13. Concurrent PFME under a supervised therapeutic plan of care.

14. Previous supervised pelvic floor muscles rehabilitation in the past 12 months for the treatment for urinary incontinence or any other pelvic floor disorder.

15. Currently taking medication to treat incontinence.

16. Impaired cognitive function.

17. Unable to tolerate use of the *Ieva* vaginal device.

8.3.3 Removal of Subjects from the Study

Subjects are free to withdraw from the study at any time for any reason.

In addition, subjects may be withdrawn from the study by the PI in consultation with the Sponsor for the following reasons:

- Subject is unable to use the *Ieva* device;
- Subject experiences a SAE;
- Protocol violation.

The clinical report will include reasons for subject withdrawals.

8.3.4 Prohibitions and Concomitant Therapy

There are no prohibited therapies, activities or medications except as described in the exclusion criteria. All medications taken by subjects during the course of the study will be recorded.

8.3.5 Meals

Due to the short duration of confinement for each study period, subjects will not be provided with a meal.

8.3.6 Activity

The subjects will be required to remain standing while performing training and in weekly tests using the *Ieva* device. The subjects are allowed to be ambulatory (i.e., no restrictions for standing, walking, sitting, or lying down) at all other times.

8.4 Treatments

8.4.1 Treatment Administered

Subjects will train twice daily for 6 (up to 8 weeks) using the *Ieva* device. The female *Ieva* Trainer will assist the subject five days a week with the training session by helping to assure that the subject is performing the training using the correct muscle movements.

8.4.2 Treatment Compliance

The *Ieva* device retains results from the subject's previous training sessions. Therefore, when the subject trains at home or when a session is missed the female *Ieva* Trainer will be able aware of the data and can counsel the subject if no session data is recorded due to a missed session.

9 STUDY PROCEDURES

The Study Events Flow Chart (Section 4) summarizes the procedures to be performed at each visit. Individual procedures are described in detail below. Additional evaluations/testing may be deemed necessary by the PI and/or the Sponsor for reasons related to subject safety.

Any nonscheduled procedures required for urgent evaluation of safety concerns take precedence over all routine scheduled procedures.

Screening visit:

This visit may be conducted in one to two visits, as needed. The study will be explained by the Study Director and the consent will be reviewed with prospective participants. The consent will be obtained by the licensed Physician Investigator or his Study Director. The study participation will be entirely voluntary.

Each subject will provide samples for drug screening, pregnancy testing, and buccal swabs for alcohol screening.

The following surveys will be administered:

- Medical, Epidemiologic and Social Aspects of Aging (MESA)
- Urinary Distress Inventory questionnaire, short version (UDI-6)
- Incontinence Impact Questionnaire, short form (IIQ-7)
- Patient Global Impression of Severity (PGI-S) Scale
- Revised Urinary Incontinence Scale (RUIS)
- Voiding diary – 24 hours intake and output and symptoms diary - to be taken home and completed within the first week of participation
- Female Sexual Function Index (FSFI) (optional)
- Pelvic Organ Prolapse/Incontinence Sexual Questionnaire (PISQ-IR) (optional)

Medical History will be obtained to include:
- Demographic data
- Height/weight
- Concomitant medication
- Latex allergy (for selection of disposable probe cover)

The female *leva* Trainer therapist will familiarize the subject with the *leva* Incontinence System™ and instruct on the technique of contraction.

The female *leva* Trainer will conduct baseline *leva* testing and measurements will include: Baseline angle; angle with Valsalva (or bear down maneuver); highest angle with pelvic floor muscles contraction; ability to sustain contraction and contractions in timed 15 seconds. This series is called the *leva* Test.

The subject will train for 2 ½ minutes using the *leva* device (*leva* Training) – each cycle will have 15 seconds of contraction with 15 seconds of relaxation. Participants will perform 5 alternating repetitions.

The female *leva* Trainer will record *leva* device measurements.

Study visits 2-30 (with the female *Ieva* Trainer):

Frequency: once a day 5 days a week. The female *Ieva* Trainer will supervise the participants on performing 2 1/2 minutes of 5 repetitions of pelvic floor exercises using the *Ieva* Incontinence System TM (*Ieva* Training)

Once a week, preferably Mondays, during the about 6-8 week study period:

The subjects will be asked to perform a series of 5 exercises "*Ieva* Test" to test the effect of the daily training and follow the test with the 2 ½ minutes of training (Ieva Training). The female *Ieva* Trainer will record Ieva device measurements.

The study participants will be given the following surveys:

- UDI-6
- IIQ-7
- PGI-S
- RUIS

At 3 weeks:

The subjects will be asked to perform a series of 5 exercises (*Ieva* Test) to test the effect of the daily training and follow the test with the 2 ½ minutes of training (*Ieva* Training). The female *Ieva* Trainer will record Ieva device measurements.

The study participants will be given the following questionnaires:

- UDI-6
- IIQ-7
- PGI-S
- PGI-I
- RUIS
- Voiding diary completion

The Study Director or PI will complete the Clinician's Global Impression of Improvement (CGI-I) evaluation.

At 6 weeks:

The subjects will be asked to perform a series of 5 exercises (*Ieva* Test) to test the effect of the daily training and follow the test with the 2 ½ minutes of training (*Ieva* Training). The female *Ieva* Trainer will record Ieva device measurements.

The study participants will be given the following questionnaires:

- UDI-6
- IIQ-7
- PGI-S
- PGI-I
- RUIS

The Study Director or PI will complete the Clinician's Global Impression of Improvement

(CGI-I) evaluation.

At the End of Study/ Early Termination visit:

The subjects will be asked to perform a series of 5 exercises (*Ieva* Test) to test the effect of the daily training. The female *Ieva* Trainer will record Ieva device measurements.

The study participants will be given the following questionnaires:

- UDI-6
- IIQ-7
- PGI-S
- PGI-I
- RUIS
- Voiding diary completion
- FSFI (optional)
- PISQ-IR (optional)

The Study Director or PI will complete the Clinician's Global Impression of Improvement (CGI-I) evaluation.

9.1.1 Adverse Events

9.1.1.1 Monitoring

Subjects will be monitored at each study visit for adverse events. A specific enquiry will be made at the time of each check-in. The subjects will be queried with an open-ended question such as "How are you feeling?" or "How have you been feeling since your last visit?"

9.1.1.2 Serious Adverse Event

Any SAE will be reported to the Sponsor and the Institutional Review Board (IRB), as required. All SAEs will be reported to the Sponsor via fax or e-mail within one working day of becoming aware of the event, whether or not the serious events are deemed study treatment-related and within 5 working days to the IRB (24 hours of discovery if the event involves a death), as required.

An SAE is any AE or suspected adverse reaction that in the view of either the PI or Sponsor, results in any of the following outcomes: Death, a life-threatening adverse event, inpatient hospitalization or prolongation of existing hospitalization, a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions, or a congenital anomaly/birth defect. Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered serious when, based upon appropriate medical judgment, they may jeopardize the subject and may require medical or surgical intervention to prevent one of the outcomes listed in the above definition.

Life-threatening is defined as an AE or suspected adverse reaction that in the view of the PI or Sponsor, its occurrence places the patient or subject at immediate risk of death. It does not include an adverse event or suspected adverse reaction that, had it occurred in a more severe form, might have caused death.

Treatment of SAEs will be performed by a physician, either at the site or at a nearby hospital emergency room. Where appropriate, medical test(s) and/or examination(s) will be performed to document resolution of event(s). Outcome may be classified as resolved, improved, unchanged, worse, fatal, or unknown (lost to follow-up).

If a SAE occurs to a subject on this study, contact the Sponsor's Representative listed in Section 2.

10 DATA ANALYSIS

Data will be handled and processed according to Operating Procedures, which are based on the principles of GCP.

10.1 Statistical Methods

Detailed methodology for summary and statistical analyses of the data collected in this study will be documented in the Clinical Study Report.

10.1.1 Determination of Sample Size

This is an open-label study where subjects serve as their own control. The sample size was selected without statistical considerations.

10.1.2 Subjects to Analyze

Safety Population: All subjects who were administered at least one training session will be included in the safety evaluations.

Efficacy Population: All subjects who had at least one *Ieva* testing administration and measurement of any of the efficacy assessments post Screening Visit.

10.2 Safety Evaluation

Safety data will be populated in individual CRFs. All safety data will be listed by subject.

AEs and SAEs will be monitored throughout the study. All SAEs will be recorded and reported. Concomitant medications and medical history will be listed by subject.

11 STUDY ADMINISTRATION

11.1 Ethics

11.1.1 Institutional Review Board

This protocol will be reviewed by Chesapeake Research Review, Inc., an IRB and the study will not start until the IRB has approved the protocol or a modification thereof. The IRB is constituted and operates in accordance with the principles and requirements described in the US Code of Federal Regulations (21 CFR Part 56). The IRB is compliant to International Conference on Harmonisation (ICH) guidelines, and may be reached at:

Chesapeake IRB
6940 Columbia Gateway Drive, Suite 110
Columbia, MD 21046
Tel.: +1 410 884 2900

11.1.2 Ethical Conduct of the Study

This research will be carried out in accordance with the protocol, US Code of Federal Regulations, GCP, 21 CFR Parts 50 and 56, the ethical principles set forth in the Declaration of Helsinki, and the ICH harmonized tripartite guideline regarding GCP (E6 Consolidated Guidance, April 1996).

11.1.3 Subject Information and Consent

The purpose of the study, the procedures to be carried out and the potential hazards will be described to the subjects in non-technical terms. Subjects will be required to read, sign and date an ICF summarizing the discussion prior to Screening, and will be assured that they may withdraw from the study at any time without jeopardizing their medical care.

Subjects will be given a copy of their ICF.

11.2 Termination of the Study

The Principal Investigator reserves the right to terminate the study in the interest of subject welfare. The Sponsor may terminate the study for administrative reasons.

11.3 Data Quality Assurance

The Principal Investigator will designate personnel responsible for implementing and maintaining quality assurance and quality control systems to ensure that the study is conducted, and that data are generated, documented and reported in compliance with the study protocol, GCP and Good Laboratory Practice requirements as well as applicable regulatory requirements and local laws, rules and regulations relating to the conduct of the clinical study.

11.4 Direct Access to Source Data/Documents

The Principal Investigator will ensure that the Sponsor, IRB and domestic and foreign regulatory authorities will have direct access to all study sites, source data/documents, and

reports for the purpose of monitoring and auditing. In the event that other study-related monitoring should be done by other parties, those parties will be required to sign a confidentiality agreement prior to any monitoring or auditing.

11.5 Study Device Supplies, Packaging and Labeling

The Sponsor will supply sufficient quantities of devices to allow completion of this study. Each subject will be provided with her own device and can retain the device at the end of the study. The device has a value of about $700. If the subject does not already own an iPhone to run the *Ieva* software they will be provided at no charge an iPOD touch ($250 value) to use. It will be up to the discretion of the Sponsor if the iPOD touch needs to be returned to the study site or can be retained by the subject at the end of the study. Records will be made of the receipt and dispensing of devices supplied. This accountability record will be available for inspection at any time. At the completion of the study, the original accountability record will be available for review by the Sponsor upon request.

11.6 Data Handling and Record Keeping

All raw data generated in connection with this study, together with the final report, will be retained for at least 5 years after completion of the final report. These documents should be retained for a longer period however if required by the applicable regulatory requirements or by an agreement with the Sponsor. It is the responsibility of the Sponsor to inform the PI/Institution as to when these documents no longer need to be retained.

11.7 Publication Policy

All unpublished information given to the Principal Investigator by the Sponsor shall not be published or disclosed to a third party without the prior written consent of the Sponsor.

The data generated by this study are considered confidential information and the property of the Sponsor. This confidential information may be published only in collaboration with participating personnel from the Sponsor or upon Sponsor's written consent to publish the article.

12 REFERENCES

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2 Herzog AR, Diokno AC, Brown MB, Normolle DP, Brock BM. Two-year incidence, remission, and change patterns of urinary incontinence in noninstitutionalized older adults. J Gerontol 1990;45:M67-M7.

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