Vesiflo™
ADVANCING PELVIC HEALTH®

Reinventing Bladder Drainage

The inFlow™ Urinary Prosthesis for Women and Guardian™ VCS

Presentation to 2nd International Congress for Underactive Bladder
Kevin M. Connolly, CEO – 4 December 2015

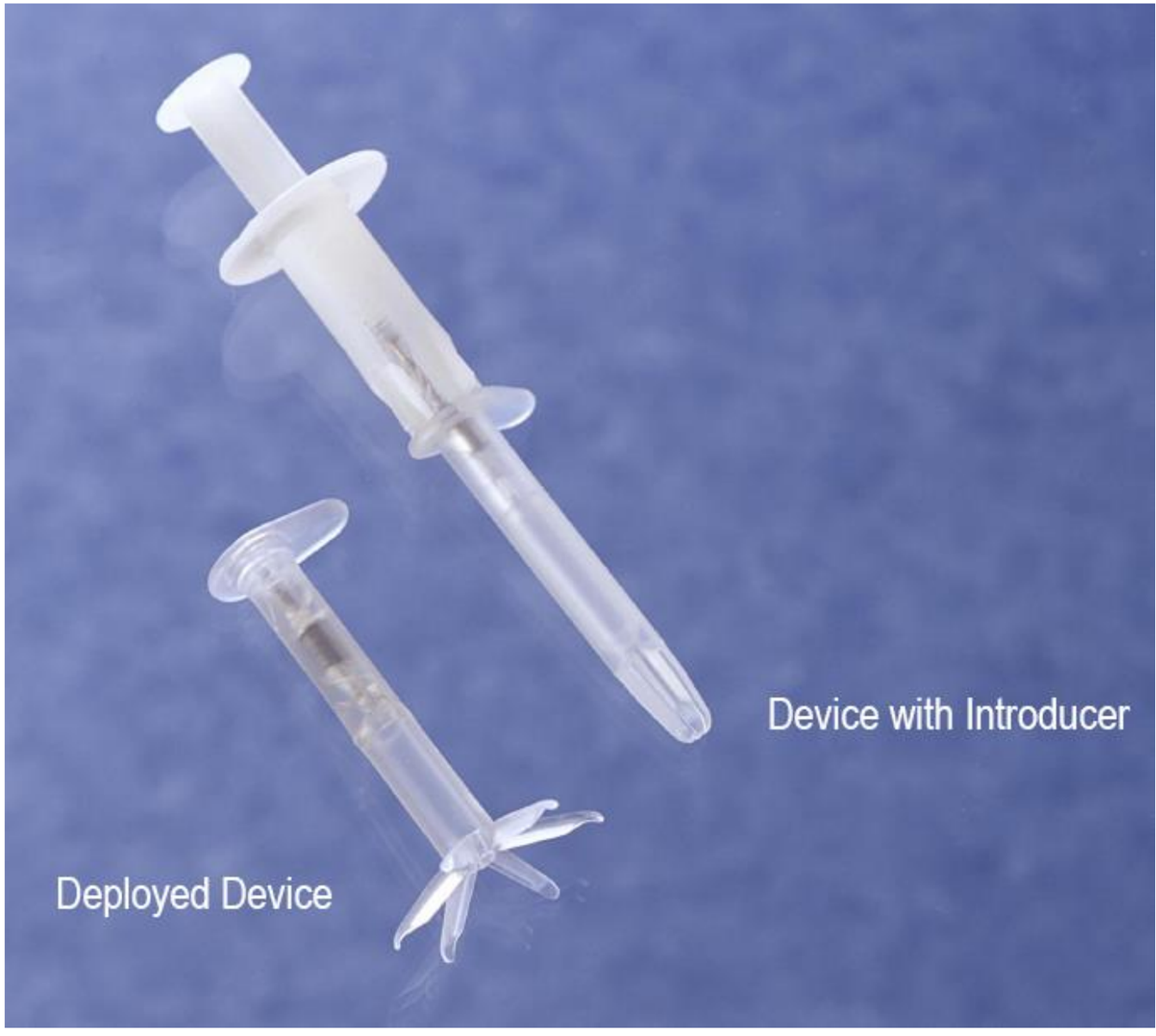
Introduction

- Although very commonly used, urinary catheters cause infections that can be life-threatening and degrade quality of life, particularly with chronic use
  - Women with neurogenic underactive bladder are most affected as this is generally an incurable condition and most now use catheters on a life-long basis
- inFlow™ is an *active* urinary prosthesis that replaces *passive* urinary catheters
  - Recently FDA approved device has superior infection resistance, improves quality of life
- Guardian™ VCS, Vesiflo's mobile health system, extends inFlow's benefits
  - Provides remote patient monitoring with clinical alerts, patient guidance and Big Data

Indication for Use

The inFlow Intraurethral Valve-Pump and Activator is a replaceable urinary prosthesis intended for use in adult females who have incomplete bladder emptying due to impaired detrusor contractility of neurologic origin

Must be replaced every 29 days



Urinary Prosthesis

- A prosthetic device is intended to compensate for a specific anatomic deficiency
- Women with impaired detrusor contractility (IDC) cannot generate bladder pressure, so the inFlow PUMPS the urine out
  - The inFlow also provides a valve that can augment sphincteric deficiency
- As a prosthetic device, inFlow's clinical objective is to normalize voiding
  - This is a far more ambitious objective than simple bladder drainage and so requires patient support/management

U.S. Women with IDC

Estimated number of U.S. women in the inFlow's target population based on types of neurologic disease and injury resulting in impaired detrusor contractility (IDC):

Primary Medical Condition	Prevalence	% Neurogenic	# Neurogenic	% Female	# Female
Spinal Cord Injury	259,000	81%	209,790	15%	31,500
Cerebral Palsy	764,000	24%	183,360	42%	74,808
Multiple Sclerosis	400,000	56%	224,000	67%	150,000
Parkinson's Disease	1,000,000	20%	200,000	40%	80,000
Stroke	4,000,000	12%	480,000	43%	206,400
Diabetes	25,800,000	2%	516,000	48%	247,680
Total Neurogenic Bladder					790,388
IDC (33% of Neurogenic)					**263,199**

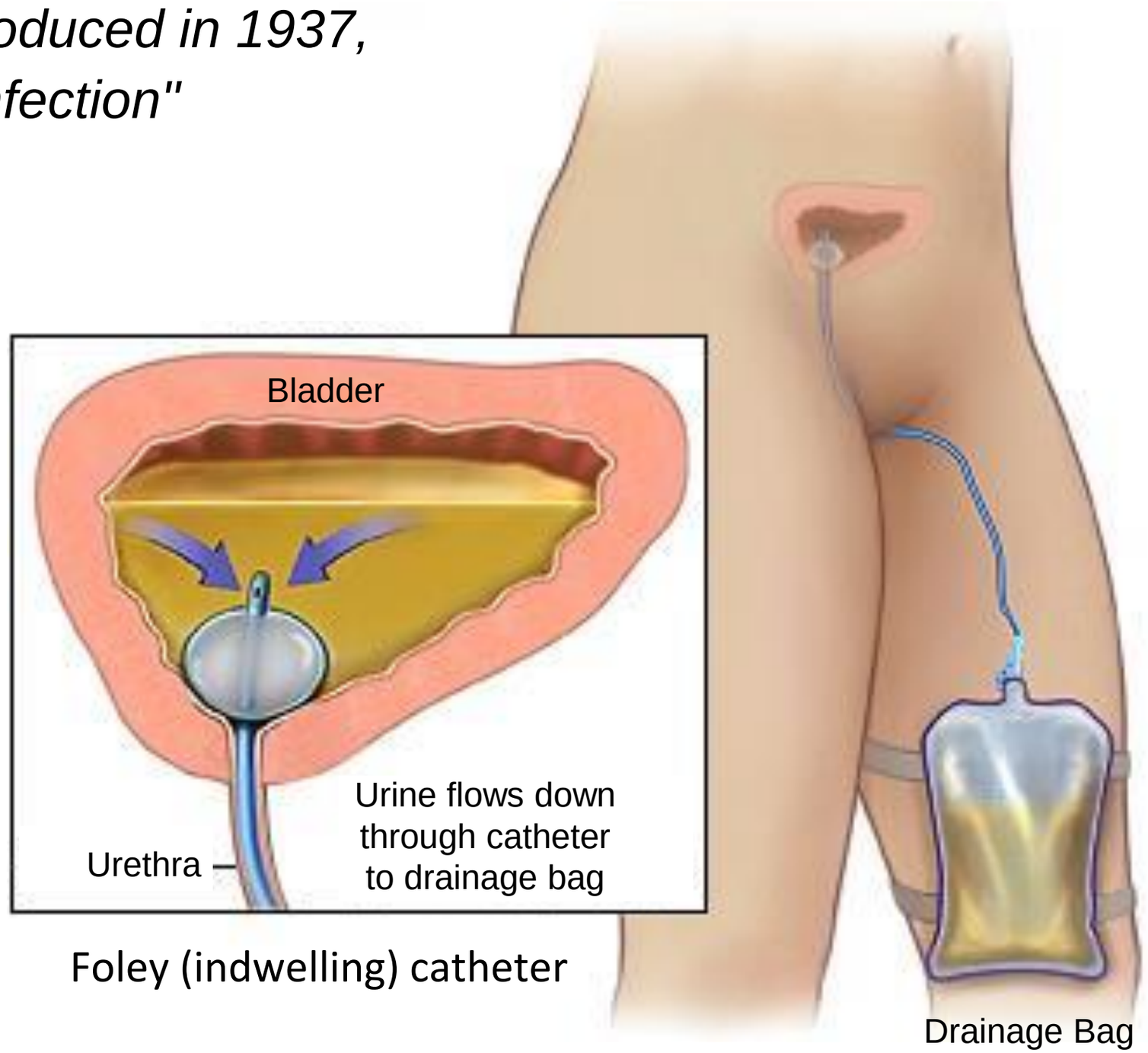
- Numbers are derived from CDC data and estimates by patient advocacy groups
- Does not include IDC of idiopathic or iatrogenic (over-use of anticholinergics, surgery, etc.) origin

Medical technology has made amazing advances in many areas

Bladder drainage is not among them

“..fundamental problems with the basic design of the catheter, which has changed little since it was first introduced in 1937, induce susceptibility to infection"

-R Feneley



Foley (indwelling) catheter

Catheter-Associated Urinary Tract Infections

*Attributable deaths estimated to be over 13,000**

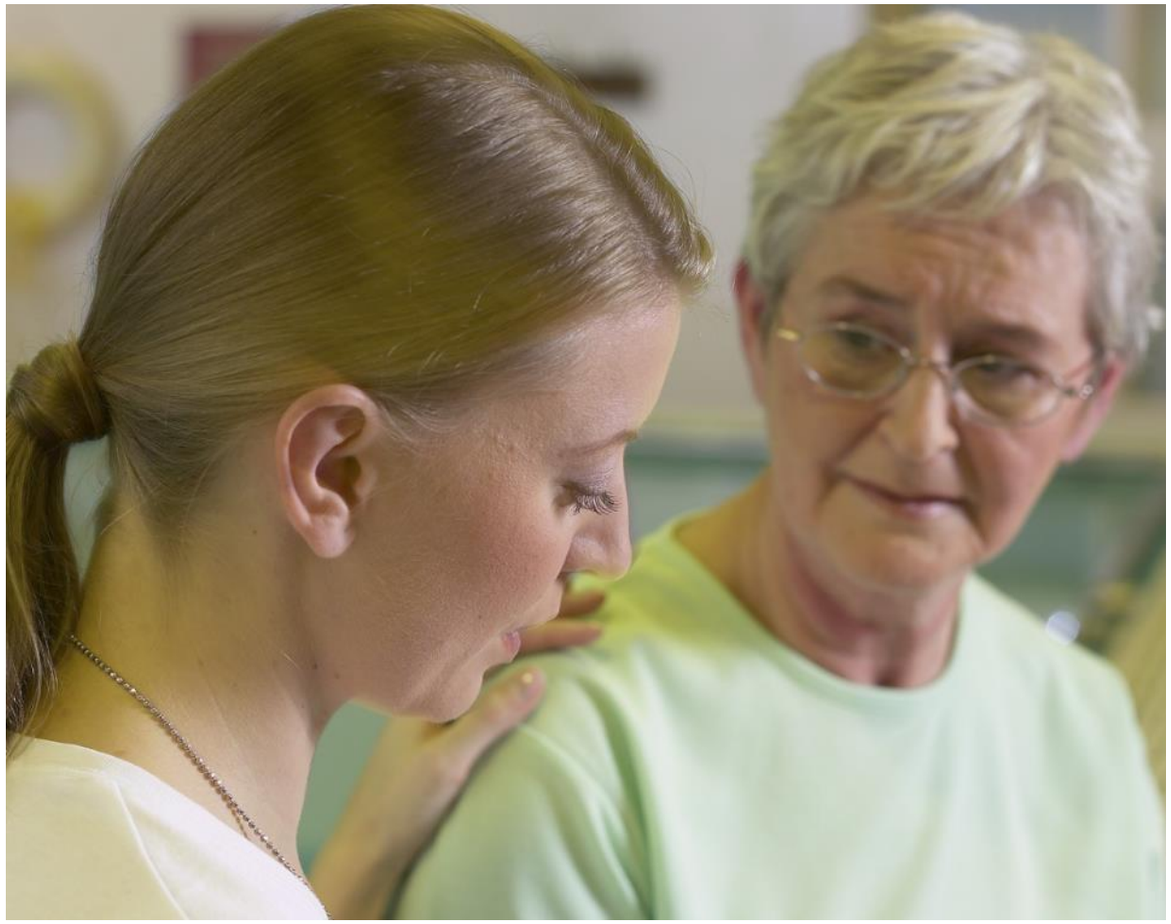
-U.S. CDC

“Antimicrobial resistance among urinary pathogens is an ever increasing problem”

* 2002 estimate for U.S. hospitals, does not include community dwelling or institutional catheter use

The Kind of Life No One Wants

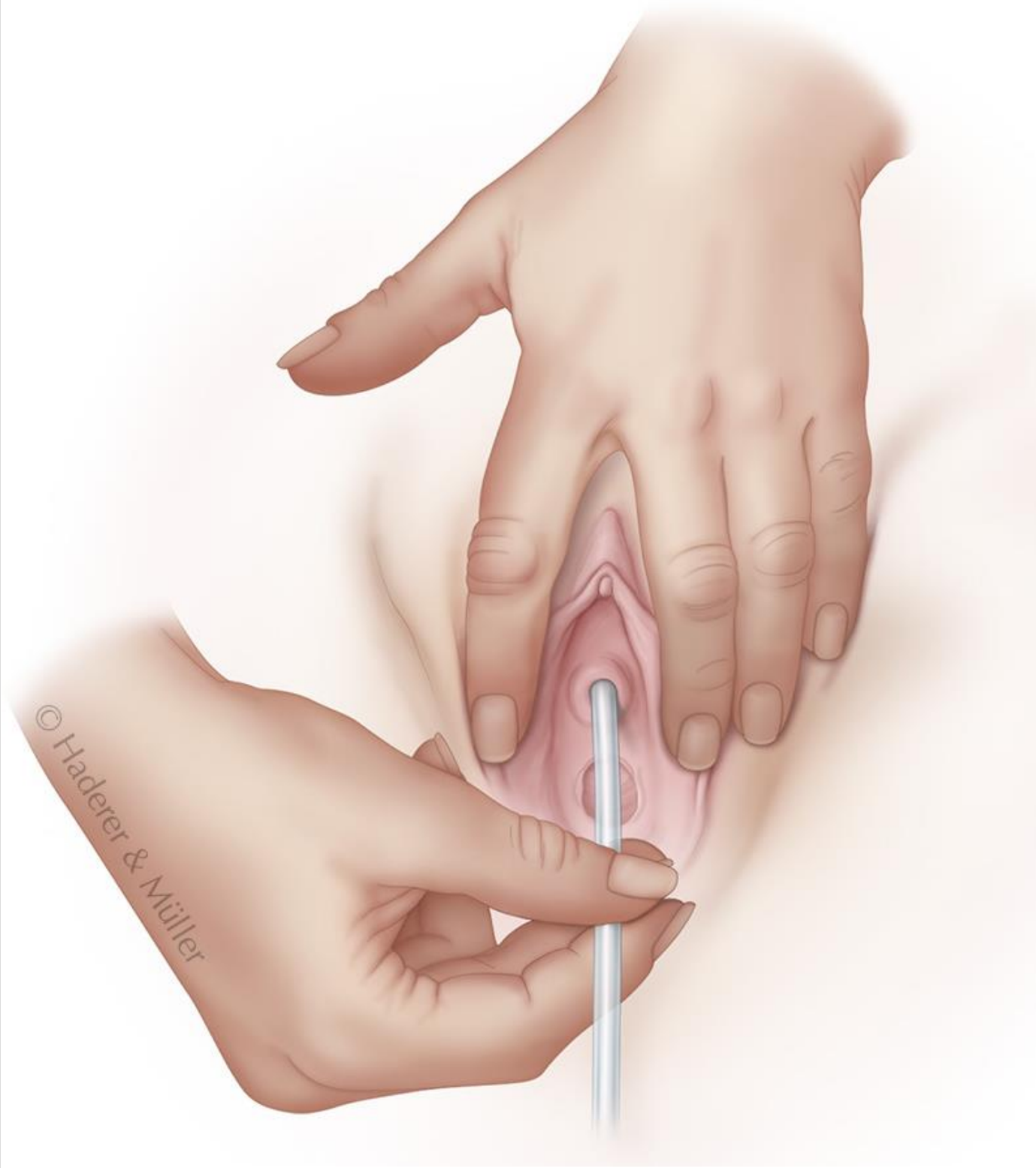
- Chronic use of urinary catheters also significantly degrades quality of life
- To understand why, you only have to consider the two most common types of urinary catheters
  - Intermittent catheters (CIC)
  - Indwelling (Foley) catheters



CIC- the current standard of care

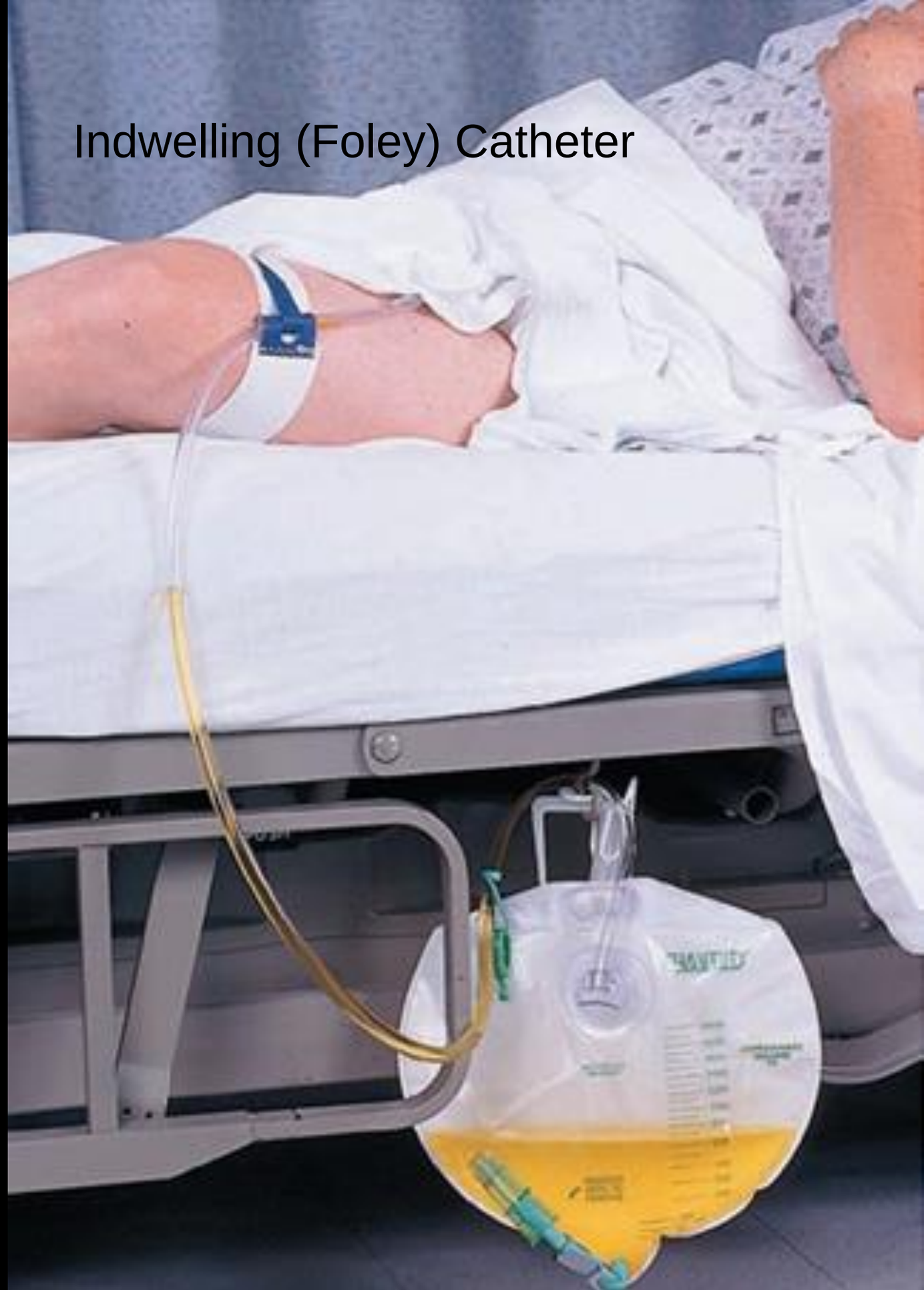
Requires insertion of tube into the bladder 4-6 times per day

Clean Intermittent Catheterization



The most common alternative to CIC

Requires being tied to a bag of your own urine

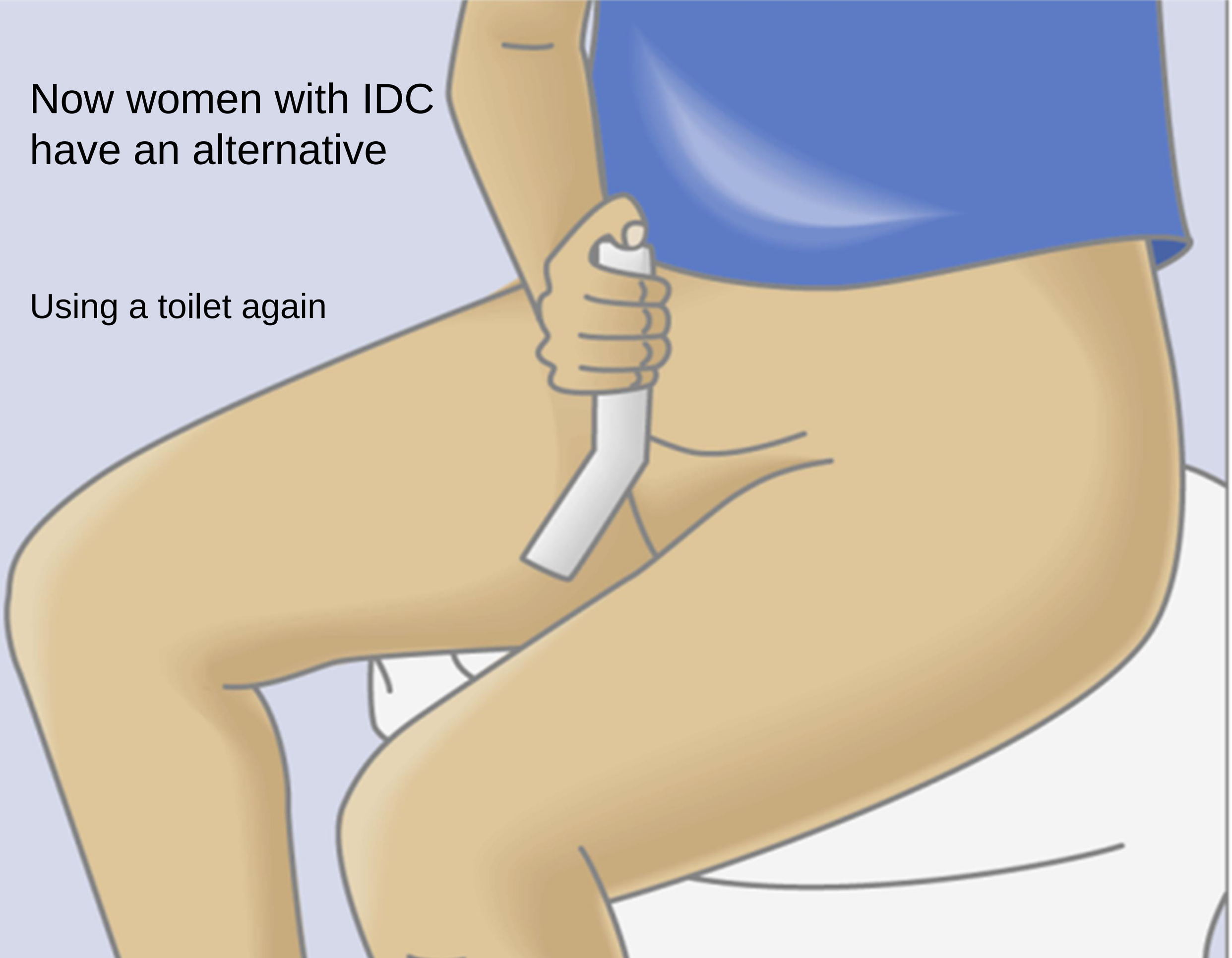


inFlow's Target Population is the Most Affected

- Catheter problems are amplified for women with impaired detrusor contractility (IDC)
  - IDC is caused by life-altering neurologic disease or injury (MS, spinal cord injury, Parkinson's, stroke, diabetes, etc.)
- IDC is generally incurable and typically <u>requires life-long catheter use</u>

Now women with IDC have an alternative

Using a toilet again

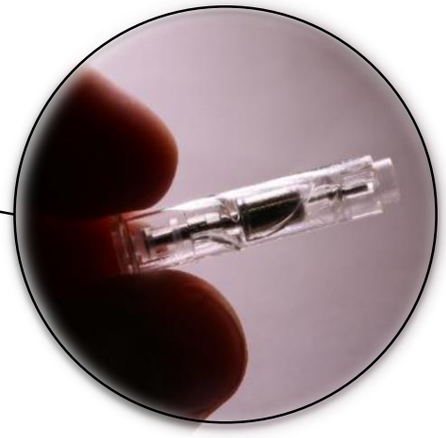


Female Urinary Prosthesis

inFlow™
RESTORING CONTROL™

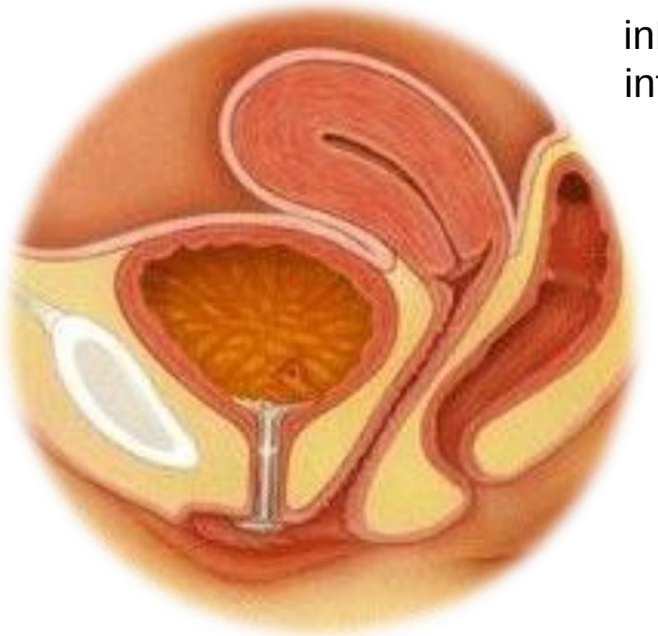
Activator remote control

inFlow device



Internal valve-pump

How the inFlow Works

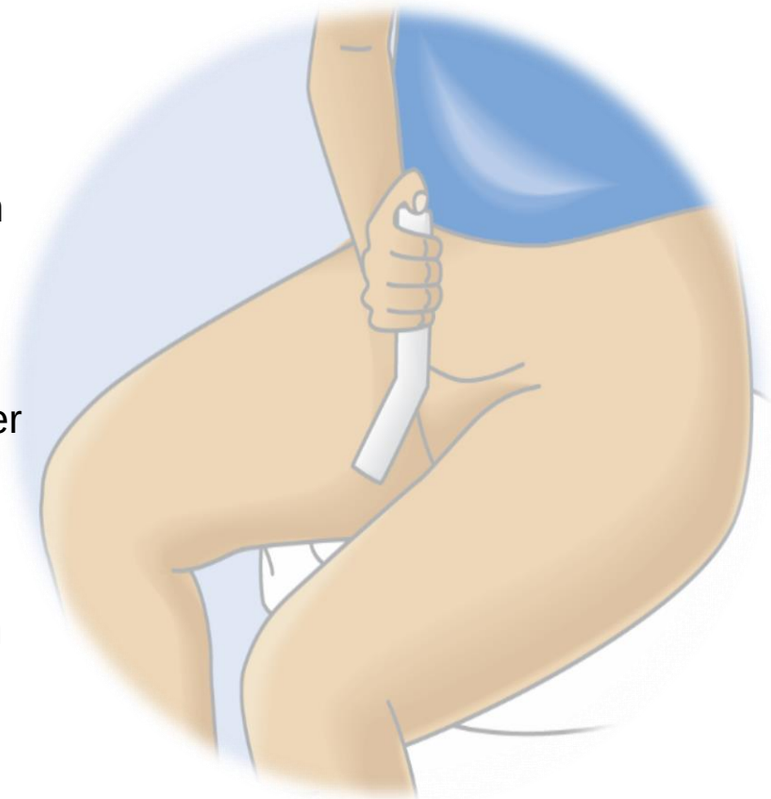


inFlow device is inserted into urethra and remains in place for 29 days

Pressing Activator button engages internal pump

Pumps urine out of bladder at a normal flow rate

Allows dignified urination on demand



Clinical Practice

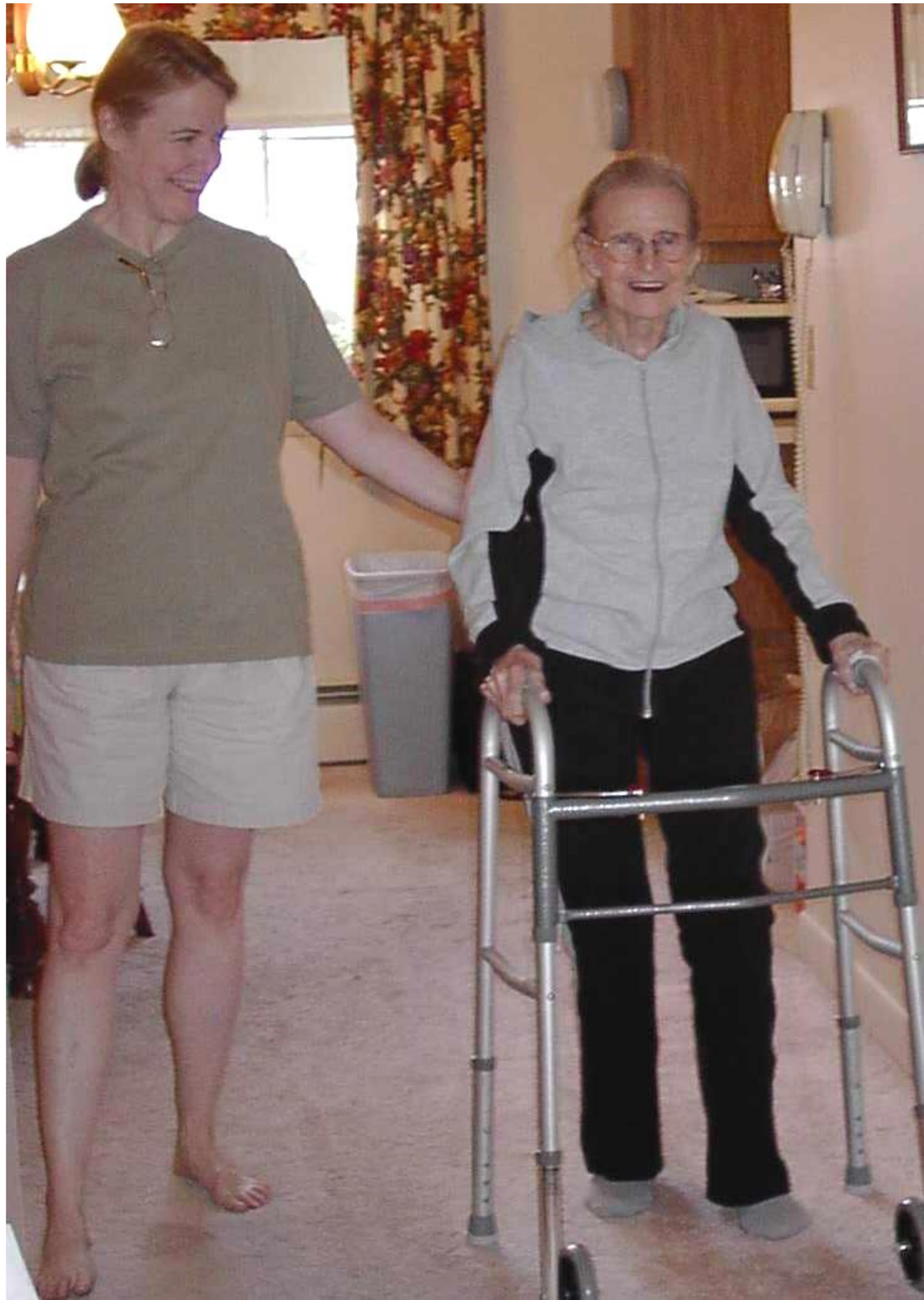
- Patient with established IDC presents herself for evaluation
- Cystourethroscopy is performed
  - Needed to assess condition of urethral sphincter, suitability for urethral insert
- Urethral length is measured with inFlow Sizing Device and recorded
  - Needed to determine appropriate size of inFlow device
- Physician inserts initial device, in-services patient and spouse or caregiver
  - Physician or nurse confirms that patient can void, use Activator correctly
  - Practice provides a point of contact for follow-up, patient questions
- Device is replaced after 29 days
  - Subsequent device insertions can often be performed by spouse or caregiver

How the inFlow Promotes Good Bladder Health

- Good bladder health requires
  - Periodic
  - Forceful and
  - Complete evacuation of urine
- Unlike urinary catheters, the InFlow mimics normal urination and maintains all of these key functions
- As a result, inFlow users can experience significant benefits

Significant Benefits

- Decreased rate of UTIs
- Dramatically improved quality of life
  - Eliminates tubes, bags
  - Normalizes toileting
  - Restores personal dignity



Clinical Evidence of Benefits

- Its pivotal trial showed the inFlow to have a lower UTI rate than CIC, the current standard of care, prompting the FDA to comment:

  "It is noteworthy that the most significant of adverse events – UTI – appears to occur at a lower rate with the inFlow device as compared to CIC. Among patients treated with the inFlow device, UTIs were stable and easily managed with antibiotics."

  –FDA News release of October 14, 2014

- Its pivotal trial also showed that inFlow improved quality of life by almost 60% compared with CIC (clinically and statistically significant)
  - The inFlow improved quality of life by 80% in an investigator-sponsored 1-year study

inFlow has been Extensively Studied

Biocompatibility	Meets current ISO 10993 standards for permanent surface device with mucosal membrane contact
Seven Clinical Studies (total *n*=501)	Six investigator-sponsored studies (total *n*=228 unique subjects) published in peer-reviewed journals, including three long-term studies of 1-4 years
	Pivotal trial (*n*=273) met all endpoints and showed 60% higher quality of life and lower UTI rate than current standard of care (CIC)
Clinical Use OUS	>1,200 women-years clinical experience, mostly in DE and AUS
Adverse Events	No serious or long-lasting AEs associated with device use reported

Encrustation Study

- An *in vitro* study *by* Stickler *et al* showed inFlow's encrustation resistance to be **at least 8.4x superior** to an all-silicone Foley, the current gold standard:

  "Under conditions that simulated a heavy infection of P. mirabilis, where a conventional Foley catheter blocked with crystalline biofilm after 25.7 hours, the inFlow device drained the bladder for at least 9 days… (and its) central lumen appeared to be essentially clear."

- No encrustation was reported in inFlow's pivotal trial

Pivotal Trial Design

- 18-site study (*n*=273) to compare safety, effectiveness and patient satisfaction of the inFlow device versus clean intermittent catheterization (CIC)
  - CIC is current standard of care for long-term bladder drainage
  - Study limited to women with atonic bladder who were already using CIC
  - Single-arm crossover design in which each subject acted as her own control
  - CIC use tracked for 8 weeks as Baseline, then switched to inFlow Treatment for 16 weeks
- Relevant clinical endpoints were selected
  1. Primary Endpoint: Post-void residual (PVR) - indicates how effectively each device performs its primary function, draining the bladder
  2. Secondary Endpoint: Quality of life per Wagner I-QOL - indicates effects of using these highly personal devices
  3. Comparative Safety: Adverse events, particularly UTI rate

Pivotal Trial Results

- All clinical endpoints were met

1. **Primary Endpoint: Post-void residuals (PVRs)** - CIC and the inFlow were equivalent in their ability to fully empty the bladder
   - 98% (113/115) of evaluable subjects had comparable PVRs, with median PVR at each visit during inFlow Treatment ranging from 10-20cc (1-sided exact 95% confidence lower limit: 95%; 2-sided exact 95% confidence interval 94% - 99.8%).
   - 92-99% of all subjects had comparable PVRs at every treatment visit ($p<0.0001$)
2. **Secondary Endpoint: Quality of life per Wagner I-QOL** – the inFlow was superior to CIC in its affect on quality of life
   - Scores were almost 60% higher for the inFlow than for CIC ($p<0.0001$)
3. **Comparative Safety:** Adverse events were generally comparable and no significant or long-lasting AEs associated with inFlow use were reported, but two notable findings
   - ~50% of subjects failed to complete study due to discomfort and/or leakage
   - UTI rate same or better than for CIC, even though inFlow is 24/7 device

UTI Rate

- As an indwelling device, inFlow was expected to have a higher UTI rate than intermittent catheters
- Instead, per subject-month rates for subjects completing the study declined with continued inFlow use
  - CIC Baseline=0.12, first half of inFlow Treatment period=0.11 and second half of inFlow Treatment Period=0.08
- UTI experience in pivotal constitutes a representative and robust estimate of device performance in clinical practice
  - Based on 417 patient-months cumulative exposure in 157 patients

Device Acceptance

- ~50% of subjects failed to complete pivotal trial due to device awareness/ discomfort, leakage – many dropped out within 1-4 days
  - Device awareness is usual with new foreign body (like tampons or contact lenses)
  - Leakage can be caused by spasm, but also by incorrect use of Activator
- Many patients accommodate to device immediately or within 1-2 weeks, others need more help
- Nursing support shown to be effective in increasing device success
  - Lynch *et al* provided active nursing support and reported almost no device-related dropout in 1-year study (*n*=21)

Support

- Vesiflo is developing multiple levels of support for clinicians and patients
  - Online CME-type courses
  - On-site clinical in-servicing
  - Videos for patient instruction and peer mentoring
  - Access to Guardian™ Voiding Care System (VCS)
- Role of the Guardian VCS* is to provide active, ongoing patient support
  1. Remote patient monitoring with alerts
  2. Patient guidance
  3. Big data to improve care

* Currently in development

1. Remote Patient Monitoring with Alerts

- New “smart” Activator measures voided volume each time device is used
  - Low volume can be an indicator of compliance or health issues and warrants investigation

Each time its button is pressed, Activator calculates voided volume

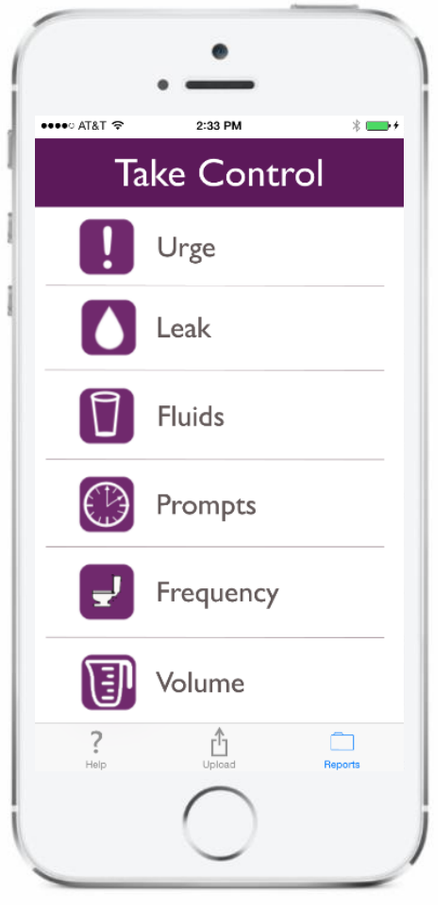
Data are routinely transmitted to iOS app and sent to cloud

No patient initiative required

If voided volume is low, clinician or caregiver can be alerted

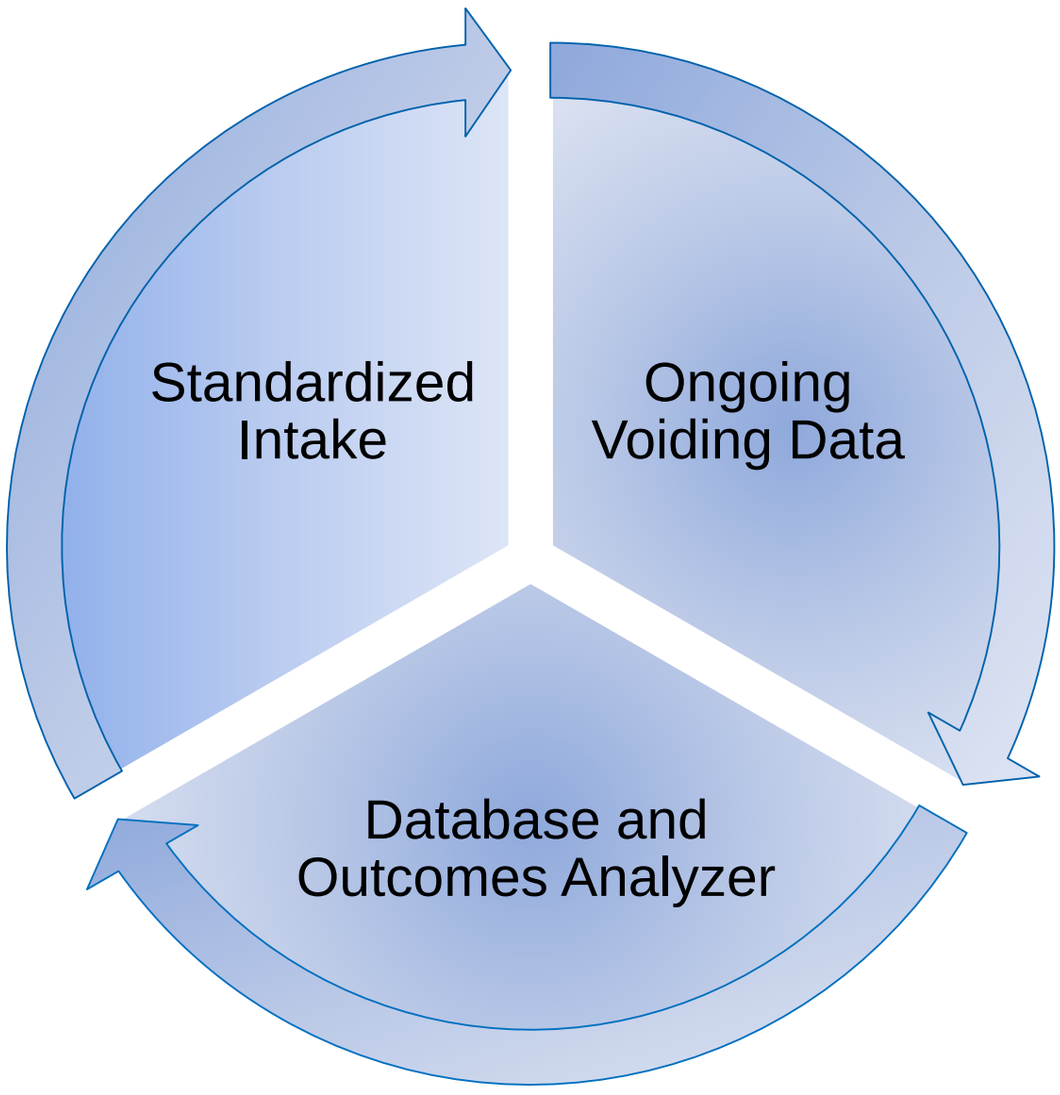
2. Patient Guidance

- Proper hydration and routine voiding are critical for bladder health
- The Take Control™ app for iOS devices* prompts patients to void per schedule and meet hydration goals
  - Default settings can be adjusted by clinician
  - Optional tracking of compliance to prompts



* Use of Apple Health assists in compliance with data security, etc.

3. Big Data to Improve Care



Guardian VCS

Guardian VCS intended to be a controlled data environment for post-market analysis

1. Starts with a detailed standardized intake (VENUS™ in development)
2. Continues with ongoing voiding data
3. Outcomes will be analyzed to tease out intake factors and interventions associated with improved outcomes
   - Will also inform ways to improve patient retention

Adding to the Armamentarium

- The inFlow is an alternative to any type of urinary catheter
  - For CIC users, inFlow shown to improve quality of life by 60-80%
  - For Foley users, provides safety and effectiveness comparable to CIC
- Also, although CIC is a good option, many cannot or will not self-catheterize
  - Primary medical condition of those with IDC often compromises ability to self-cath
  - Many women, elderly particularly, are reluctant to repeatedly touch genital area
- These women would generally be relegated to Foleys or suprapubics, but many can use the inFlow
  - The inFlow will provide them with safety and effectiveness comparable to CIC

The Best Treatment for Infection is Prevention

- Wo
- Of t (53,323)
  -
- UTI

- As many as 40% of them died as a result (1,066 women)

Summary

- The inFlow is an *active* urinary prosthesis that can replace *passive* urinary catheters for women with IDC
  - As a prosthetic device, inFlow's clinical objective is to normalize voiding
- The inFlow is a unique solution to an age-old problem: *How to remove urine from the bladder without causing infection*
  - Infection resistance shown to be superior to current standard of care
- inFlow is not suited to all women with IDC, but has excellent safety profile and can transform lives
  - Mimics normal urination, restores personal dignity

Thank You

"The inFlow device is truly remarkable in its ability to virtually restore the functional behavior of the urinary bladder. No other product, drug, or device can accomplish this to the same degree. The device should be given a high priority consideration for all female patients having difficulty emptying their bladders." -R Schmidt, MD

Contact:
Kevin M. Connolly, CEO
M (425) 985-8418
kmc@vesiflo.com