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A patient centric review of the experiential & clinical data associated with the safety, efficacy, tolerability & usability of the Novoglan foreskin tissue expander to treat uncomplicated phimosis - post marketing surveillance program

Introduction:

A market review of foreskin tissue expander devices was conducted in 2005 to assess the availability of devices to treat uncomplicated adult phimosis and to gage their efficacy, tolerability, safety and usability via targeted online survey [27].

The results were analysed and it was concluded that existing devices were inappropriate or sub optimal [27]. A wide ranging review of the literature about phimosis as well as skin stretching generally, resulted in the development of the Novoglan medical device that uses a specialised balloon to stretch the foreskin and expand the delicate tissue[28]. The product prototype was developed in 2005 and was formally launched in 2006.

This paper provides a patient centric review of the experiential and clinical data associated with safety, efficacy, tolerability and usability of the Novoglan foreskin tissue expander to treat uncomplicated phimosis, as captured in the manufacturer and sponsors post marketing surveillance program.

Phimosis:

In simple terms, phimosis refers to “a condition in which the foreskin of the penis cannot stretch to allow it to be pulled back past the glans” [1]. More technically, Cold and Taylor refer to phimosis as being characterized by a stenosis of the foreskin resulting in the inability of the prepuce to retract over the glans. They also make a distinction between pathological phimosis and physiological phimosis. Pathologic phimosis can occur at any age among uncircumcised adult men and is frequently associated with infections such as balanitis. [2]

The incidence of adult phimosis is open to conjecture as research approaches have been inconsistent, however, some authors report an incidence of around 1% [3] but the incidence of adult circumcision typically linked to phimosis has been reported as high as 15.8% in the UK [4]. Schoberlein [5] found phimosis in 8.5% of 3,000 men mostly aged 18 to 22 and representing 10.4% of the uncircumcised men. Rickwood, as well as other authors, has suggested that true phimosis is over-diagnosed due to failure to distinguish between normal developmental non-retractability and a pathological condition [6].

Male phimosis is characterized by a stenosis of the foreskin resulting in the inability of the prepuce to retract over the glans. Physiological phimosis is a condition in infants and boys which usually disappears by the age of 10 [1,2].

Pathologic phimosis can occur at any age among uncircumcised adult men and is frequently associated with infections such as balanitis, chronic inflammation, repeated catheterization, forcible foreskin retraction and injury [1]. We refer to phimosis in the absence of infection, observable inflammation, injury, other disease, and scar tissue, as “uncomplicated phimosis’.

Grading Severity of Phimosis:

To assist with a more robust understanding of efficacy of Phimosis treatments, Kikiros, Beasley and Woodward developed a grading system to diagnose the severity of phimosis. [7]

- Grade 1: full retraction of foreskin, tight behind the glans.
- Grade 2: partial exposure of glans, prepuce (not congenital adhesions) limiting factor.
- Grade 3: partial retraction, meatus just visible.
- Grade 4: minimal retraction, with minor distance between tip and glans (notably, meatus nor glans exposed).
- Grade 5: No visible retraction of the foreskin

Phimosis Treatments:

Adult phimosis can cause significant and often painful symptoms such as urinary difficulties, frequent infections or ballooning of the foreskin during urination, sexual disfunction, disfigurement, pain during sex, mental health issues and partner dissatisfaction have all been documented in the literature [8].

The most common treatment for adult phimosis is circumcision [9].

Marco and Heil [10] conducted a review in support of circumcision and concluded that there was no consensus on whether or not circumcision resulted in more side effects than benefits. Their report covers the impact on infant circumcision on adult sexual function. However, In a very large study of 5552 people, reported by Frisch and Lindholm [11], they concluded that Circumcision was associated with frequent orgasm difficulties in men and with a range of frequent sexual difficulties in women, notably orgasm difficulties, dyspareunia and a sense of incomplete sexual needs fulfilment. McMahons [12] review of disorders of orgasm and ejaculation in men, reported that circumcised men were three times more likely than uncircumcised men to experience frequent orgasm difficulties which, according to an international expert panel, are either psychogenic or due to reduced penile sensitivity.

Bronselaer and colleagues [13], describe reduced penile sensitivity and sexual satisfaction subsequent to circumcision have been described by in a large cohort of 1,369 men of whom 1,059 were uncircumcised and 310 circumcised who reported less sexual pleasure than uncircumcised men.

A preliminary review of the literature results in dozens of studies referring to the adverse outcomes associated with circumcision and a summary is included in Table A

Table A - Reported Adverse Circumcision Outcomes

Authors	Adverse Circumcision Outcomes
Friedman and colleagues [9]	postoperative complications can involve pain, wound infection, edema, urinary retention, meatal stenosis, foreskin adhesion and fistulas
Adrienne Carmack [14]	bleeding, pain, meatitis, various surgical complications, delayed complications such as adhesion or skin bridges and infection notably associated with antibiotic resistant strains of Staphylococcus aureus.
Williams and Kapila [15]	Death, Bleeding, Infection, Loss of Skin/Wound Dehiscence, Trapped/Concealed Penis, Redundant Foreskin/Circumcision Revision, Preputial Adhesions/Skin Bridges, Meatitis/Meatal Stenosis, Urethrocutaneous Fistula, Glanular Necrosis/Glanular Amputation, Hypospadias
Gerharz and Haarmann [16]	Bleeding, injury to glans
Fekete and colleagues [17]	44% incidence among 48 men referred to them with dissatisfied results from an adult circumcision. Other complications included scar wrinkling (27%), redundant foreskin (23%) and paraphimosis (6%)

There is a major gap in our understanding of the consequences of adult circumcision on psycho-emotional impacts on patients. Carmack [14] identified that published studies on circumcision fail to report on this aspect or the aesthetic trauma of circumcision. However, there are clear descriptions [17] provided in the literature confirming patient anxiety following unsatisfactory adult male circumcision.

The area of medicolegal cases arising from circumcision is poorly documented in the scientific literature [16]. However, a google [18] search returns volumes of articles regarding the matter.

The impact of circumcision on a man's partner is an emerging and important area of investigation. Bensley and Boyle [19] provided the following abstract which highlights the need for a more rigorous academic investigation into this critical aspect of sexual fulfilment:

“Circumcised and genitally intact men, as well as female and gay partners having sexual experience with both circumcised and intact men, were surveyed in order to investigate the long-term effects of infant circumcision. Both circumcised men and the sexual partners of circumcised men reported a number of adverse physical, sexual, and psychological sequelae.

Logistic regression analysis revealed that circumcised men could be reliably classified as having penile scarring, need for use of lubrication when undertaking sexual activity, reluctance to use condoms, progressive decline in sexual sensitivity, as well as unhappiness with and reluctance to think about their circumcision status. Female and gay sexual partners reported that their circumcised partners were more likely to experience reduced sexual sensation as compared with their intact partners, as well as dissatisfaction with their orgasms and a wide range of negative emotions associated with being circumcised.

Evidently, there are many adverse physical, sexual and psychological effects from infant circumcision, which need to be acknowledged in any discussions pertaining to informed consent in relation to circumcision surgery”

Other treatments include topical steroids, manual stretching and foreskin tissue expansion.

Gillatt & Chung [20] describe manual stretching of the foreskin with topical cortico-steroid creams in order to minimise the symptoms of adult phimosis. They assert that this conservative initial treatment preferred by many clinicians and patients as an alterative to the higher side effects of adult male circumcision, has a poor efficacy. This treatment was first described in the literature in the 1990’s [6] and further described elsewhere [21-22]. Gillatt and Chung [17] report that the treatment is usually provided over a period of 4 to 8 weeks. Once the cream is applied to the foreskin, a progressive stretching of the prepuce over the glans can be undertaken with fingers or a skin retractor, in order to facilitate foreskin tissue expansion over time.

In there clinical experience this treatment has poor and variable efficacy often leading to circumcision with the significant problem of adverse events and outcomes as discussed above... In 2016, Gillatt and team began offerring different form of conservative treatment, the Novoglan product. This product has received generated an excellent safety profile and very high patient satisfaction rates. This is now considered a suitable alternative to circumcision or steroid creams in cases of adult phimosis. the team have initiated an independents clinical trial into the safety, efficacy and tolerability pf the Novoglan product.

The Novoglan Foreskin Tissue Expander:

The Novoglan foreskin tissue expander product is manufactured and distributed by Platigo Solutions Pty Ltd in Sydney, Australia [23] . Novoglan is indicated for use by patients 18 years and over for the treatment of phimosis or preferential loosening of the foreskin. The Novoglan devices uses a balloon system to apply pressure under the foreskin and applies distributed pressure. Persistent

treatment results in foreskin cell proliferation as an adaptive response leading to increased foreskin tissue and a looser foreskin permitting safe retraction for most patents.

A new generation liquid molded medical grade silicone foreskin stretching balloon has been developed for the specific purpose of stretching the foreskin[24]. Novoglan is designed to provide relief for tight foreskin in adults within 6 to 8 weeks. A significant number of patients have described normal retraction occurring after 14 days of continuous treatment twice per day [25].

Methodology:

A questionnaire was randomly sent to 9700 registered customers (emails) who had purchased the Novoglan foreskin tissue expander device . The recipients were de-identified. A total of 879 responses were received via the confidential online survey tool, with 68 responses being rejected for material incompleteness and 811 were included in the analysis. Of the 8821 that did not respond, they received a followup email survey with one question. 119 responses were received from the second attempt.

The questions have been grouped into tables and graphs and are described in the results section below.

Results

Table 1 - Use of instructions, device version, usability, expectations, experience, reuse.

Question	Yes	No	Undecided	Yes	No	Undecided
Did you use the Novoglan foreskin tissue expander as per the instructions	803	5	3	99.01%	0.62%	0.37%
Did you use the Novoglan foreskin tissue expander with the air plunger ?	334	463	14	41.18%	57.09%	1.73%
Did you use the Novoglan foreskin tissue expander with the squeeze bulb and stop cock?	463	334	14	57.09%	41.18%	1.73%

Did you use the Novoglan foreskin tissue expander with both the air plunger and the stop cock?	8	793	10	0.99%	97.78%	1.23%
Did you find the Novoglan foreskin tissue expander difficult to use?	82	713	16	10.11%	87.92%	1.97%
Did the Novoglan foreskin tissue expander treatment meet your expectations?	641	124	46	79.04%	15.29%	5.67%
Did you have a positive experience using the Novoglan foreskin tissue expander ?	721	81	9	88.90%	9.99%	1.11%
If your phimosis returned, would you use the Novoglan foreskin tissue expander again	663	76	72	81.75%	9.37%	8.88%

Graph 1:

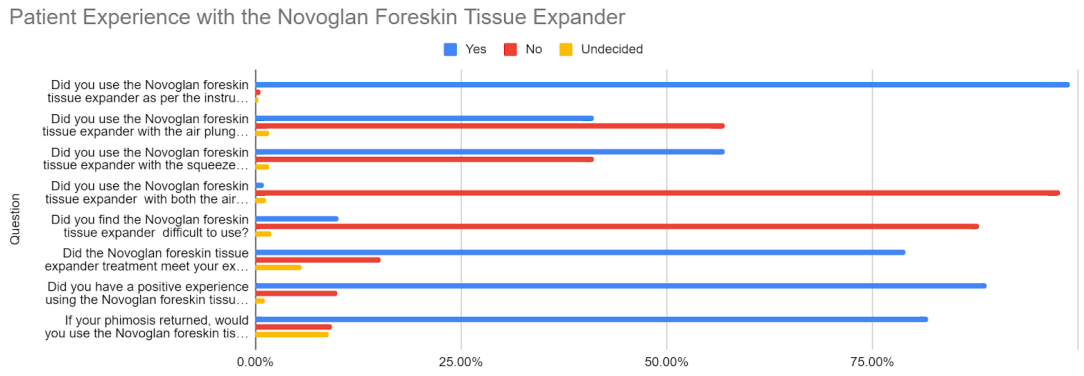
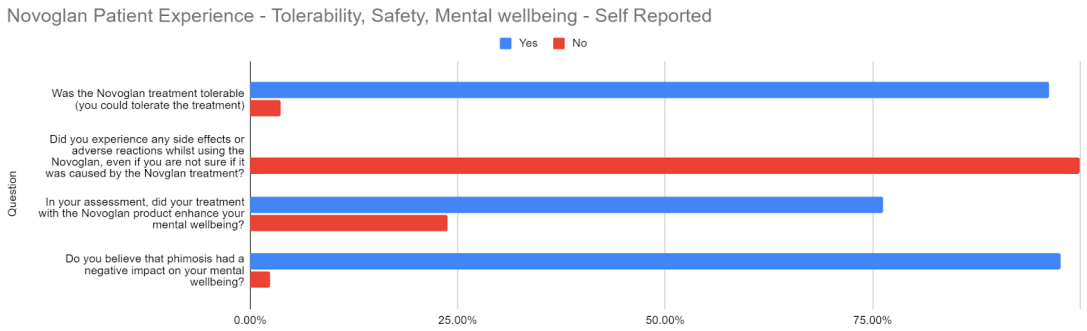


Table 2 - Tolerability, Safety & Mental Well-being

Question	Yes	No	Totals
Was the Novoglan treatment tolerable (you could tolerate the treatment)	781	30	811

Did you experience any side effects or adverse reactions whilst using the Novoglan, even if you are not sure if it was caused by the Novoglan treatment?	0	811	811
In your assessment, did your treatment with the Novoglan product enhance your mental wellbeing?	618	193	811
Do you believe that phimosis had a negative impact on your mental wellbeing?	792	19	811



Graph 2 (above)

Table 3 - Novoglan User Satisfaction / Dissatisfaction

Question	Very Unsatisfied	unsatisfied	indifferent	satisfied	very satisfied	Very Unsatisfied	unsatisfied	indifferent	satisfied	very satisfied
How satisfied were you with the Novoglan foreskin tissue expander device in	19	48	24	684	36	2.34%	5.92%	2.96%	84.34%	4.44%

treating your phimosis?										
How satisfied were you with your treatment outcome when using the Novoglan foreskin tissue expander device.	19	48	19	689	36	2.34%	5.92%	2.34%	84.96%	4.44%
How satisfied were you with the ease of use of the Novoglan foreskin tissue expan	16	52	27	691	25	1.97%	6.41%	3.33%	85.20%	3.08%

der device ?										
How satisfied were you with the overall experience with using the Novoglan foreskin tissue expander device ?	18	47	29	693	24	2.22%	5.80%	3.58 %	85.45%	2.96 %

Graph 3

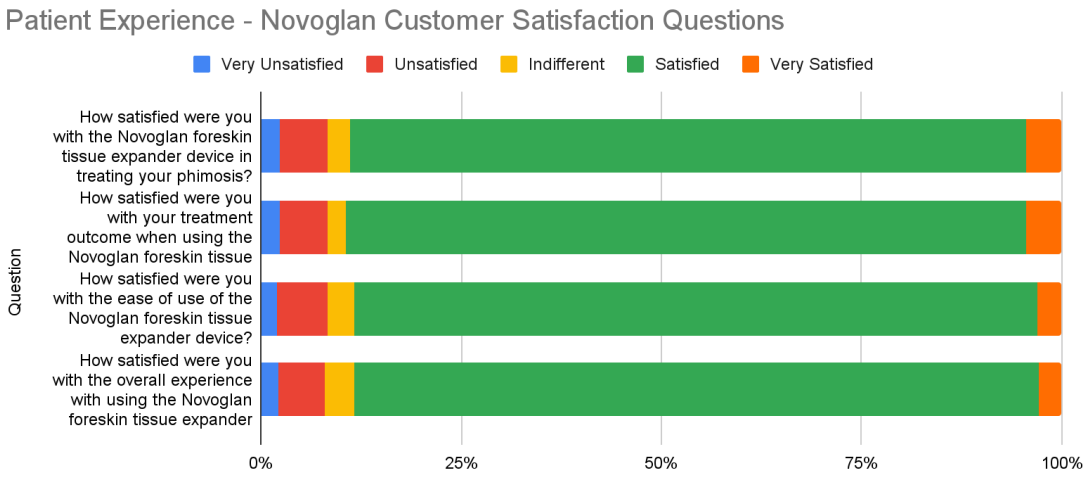


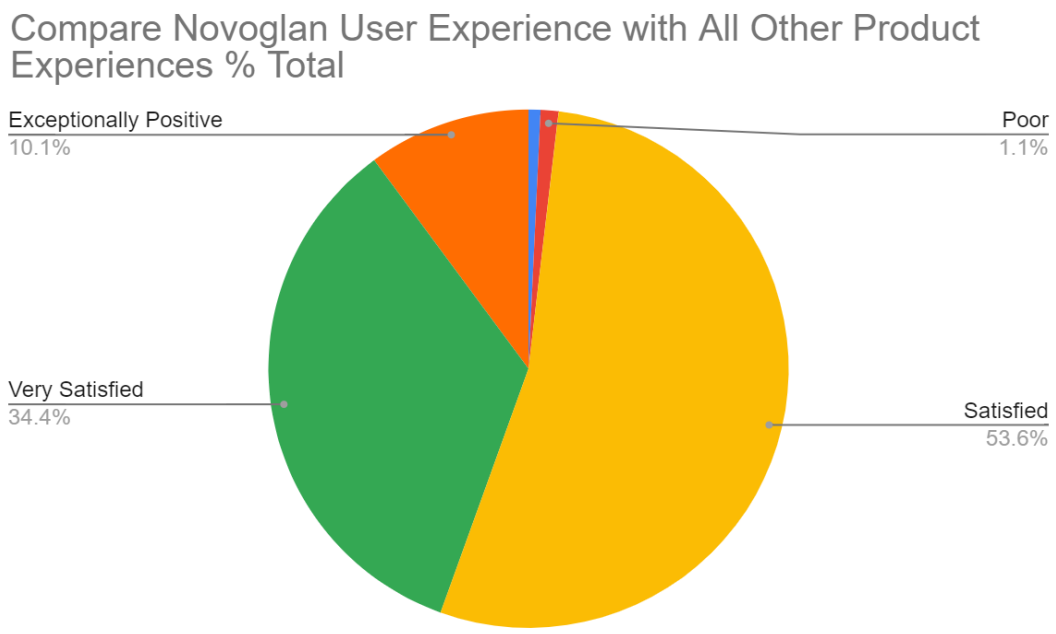
Table 4 - Reason for not responding to initial survey request

To help us with our quality control for future surveys, we would be grateful if you could please select one of the following reasons (the most important one) for not responding to our questionnaire about the Novoglan foreskin tissue expander	missed the survey email	generally do not respond to email surveys	wasn't interested	product didn't work	not satisfied with product	not satisfied with service	satisfied with product	none of the above	Total
Total #	14	62	12	3	5	6	11	6	119
% of total	11.76%	52.10%	10.08%	2.52%	4.20%	5.04%	9.24%	5.04%	100.00%

Table 5 - Comparison of Patient Experience with Novoglan Products and Service verses all their other online product and service experiences.

When you consider any or all of the products and services you have EVER purchased over the internet can you please compare how satisfied were you with the Novoglan experience (that is how would you compare the Novoglan experience to all your other online product and services experiences)?	Very Unsatisfied	Poor	satisfied	very satisfied	Exceptionally Positive	Total
Total #	6	9	435	279	82	811
% Total	0.74%	1.11%	53.64%	34.40%	10.11%	100.00%

Graph 4



Discussion

Limitations of both email based questionnaires and the survey instruments as we have used in this study have been described in the literature [26]. Furthermore it is noted that dichotomous and scaled responses options as used in this study, have their limitations. That being said, they remain an important and well established mechanism to collect data for evaluation [26].

It is well documented that survey response rates are often very poor, and there can be affirmation bias or other biases that stimulate respondents to participate [26] . In this study, we have used neutral language in the questions to reduce any unintended biases. We also followed up non respondents with a single question requesting a single reason for their lack of participation. From Table 4 we note that of the initial 8821 non respondents, 119 responded to the follow up single question survey. 62% of this group stated they either didn’t generally respond to surveys or were not interested. Only 11% provided negative reasons related to the Novoglan product or service, in that the product didn't work, they were not satisfied with the product, or they were not satisfied with service. 9% were satisfied with the product. We infer from this data that the bulk of the non respondents in total do not generally participate or are not interested in the survey and that they are not driven by either satisfaction or dissatisfaction with the product or service. We suggest this reduces the risk of significant bias for or against the product or service by the initial respondents.

From Table 1 it can be summarised that just over half the respondents had used the Novoglan Kit with the squeeze bulb and stop cock system. 10% found the product difficult to use, however, it is unclear if that was to do with the older kit that uses the air plunger. The Squeeze bulb system was introduced to enhance

usability [27] . Around 80% of respondents indicated that the novoglan device met their treatment expectations, had a positive response to the Novoglan device, and would reuse the device again if the phimosis returned. Compliance with instructions was over 99%. This data can be extrapolated to allow an interpretation that the Novoglan device in general, meets patients expectations, is easy to use as per the instructions and most users would use the device again should the phimosis return.

From Table 2 we note that no adverse events or side effects were reported. This is a very remarkable result given it is common for treatments to have some side effects or adverse events reported, even if not caused by the treatment. We undertook a literature review to identify any reported or known side effects or adverse events associated with the use of the Novoglan foreskin tissue expander. No reports were located. This result alone highlights the key safety profile that the Novoglan product has developed over the 15 years on the market. Furthermore over 96% of respondents reported that they tolerated the treatment whilst 97% reported that phimosis had a negative impact on their mental well being. The fact that over 76% of respondents reported that Novoglan treatment enhanced their mental well-being provides strong evidence that Novoglan has a positive impact on the overwhelming majority of patients treated with the Novoglan device.

From Table 3 we note that over 88% of all respondents were either satisfied or very satisfied with novoglan treatment, outcomes, ease of use, and experience of using the Novoglan device. Indifference or dissatisfaction with the Novoglan device is less than 15% across the range of questions. This data can be interpreted as almost 9 out of 10 Novoglan users were satisfied with their Novoglan experience. The data from Table 5 also supports the positive patient experience with Novoglan. In fact, nearly 90% of users rated their experience with the Novoglan product or service as “satisfied”, “very satisfied”, or “extremely positive”, when compared to all their other online purchases of services or products. This data is even more compelling when it is received with the understanding that customers that have had a negative experience are significantly more likely to speak up and provide a poor review.

Conclusions

Real world data demonstrates that the Novoglan foreskin tissue expander device is a safe and well tolerated non surgical treatment for uncomplicated phimosis. User experience is significantly positive with respect to the treatment of phimosis and the overall user experience with the device and the related service.

With extremely high levels of patient satisfaction we conclude that the Novoglan device meets the efficacy expectations of patients and has a very significant role to play as a serious option in the non surgical conservative treatment of uncomplicated phimosis.

References

1:Wikipedia https://en.wikipedia.org/wiki/Phimosis - this article needs to be scrutinised as there is a lack of citations and missing significant information regarding foreskin tissue expansion.

2:Cold CJ and Taylor JR. The prepuce. BJU Int. 1999 Jan;83 Suppl. 1:34-44.

3: Tekgül S, Dogan HS, Hoebecke P, Kocvara R, Nijman JM, Radmayr C and Stein R. EAU Guidelines on paediatric urology. In: European Association of Urology – Guidelines. 2016 Edition – Update March 2016, pp 11-12

4Raj BP, Qureshi A, Kadi N and Donat R. How painful is adult circumcision? A prospective, observational cohort study. J Urol. 2013 Jun;189(6):2237-42.

5Schöberlein W. Significance and incidence of phimosis and smegma. Munch Med Wochenschr. 1967 Feb 18; 108 (7): 373-7.

6:Rickwood AM, Walker J (September 1989). "Is phimosis overdiagnosed in boys and are too many circumcisions performed in consequence?". Annals of the Royal College of Surgeons of England. 71 (5): 275–7. PMC2499015. PMID2802472

7:Kikiros DS, Beasley SW and Woodward AA. The response of phimosis to local steroid application. Pediatric surgery international, 1993 8: 329-332.

8: https://www.health.harvard.edu/a_to_z/phimosis-and-paraphimosis-a-to-z

9.Friedman B, Khoury J, Petersiel N, Yahalomi T, Paul M and Neuberger A. Pros and cons of circumcision: an evidence-based overview. Clin Microbiol Infect. 2016 Sep;22(9): 768-774.

10 Beatriz Bañuelos Marco & Jessica Leigh García Heil. Circumcision in childhood and male sexual function: a blessing or a curse? International Journal of Impotence Research volume 33, pages 139–148 (2021)

11Morten Frisch, Morten Lindholm, Morten Grønbæk, Male circumcision and sexual function in men and women: a survey-based, cross-sectional study in Denmark†

International Journal of Epidemiology, Volume 40, Issue 5, October 2011, Pages 1367–1381, https://doi.org/10.1093/ije/dyr104

12 Chris G. McMahon MB, BS, FACSHP, Carmita Abdo MD, Luca Incrocci MD, Michael Perelman PhD, David Rowland PhD, Marcel Waldinger MD, Zhong Cheng Xin MD

, Disorders of Orgasm and Ejaculation in Men

13 Bronselaer GA, Schober JM, Meyer-Bahlburg HF, T'Sjoen G, Vlietinck R and Hoebeke PB. Male circumcision decreases penile sensitivity as measured in a large cohort. BJU Int. 2013 May;111(5):820-7.

14 Carmack A. Complications of circumcision. Online referencing http://www.doctorsopposingcircumcision.org (2016, accessed 15 June 2018).

15 Williams N and Kapila L. Complications of circumcision. Br J Surg. 1993 Oct;80(10): 1231-6

16 Gerharz EW and Haarmann C. The first cut is the deepest? Medicolegal aspects of male circumcision. BJU Int. 2000 Aug;86(3):332-8.

17 Ferenc Fekete1, Alexander Török, Peter Nyirády Revisions after unsatisfactory adult circumcisions. Int Urol Nephrol 2011 Jun;43(2):431-5. doi: 10.1007/s11255-010-9820-x. Epub 2010 Sep 29.

18 google search on medicolegal circumcision “medico legal articles about circumcision”

https://www.google.com/search?q=medico+legal+artic...

19Gillian A. Bensley and Gregory J. Boyle Bond University. Gold Coast. Queensland. Australia Gillian A. Bensley. Physical, Sexual, and Psychological Effects of Male Infant Circumcision. A New Preputial Structure

20 Gillatt D, and Chung E. Novoglan-01 clinical trial of a conservative treatment for adult

Phimosis. Macquarie University Sydney NSW Australia 2109 - Submitted for publication

21 Garcia de Freitas R, Nobre YD, Demarchi GT, Hachul M, Macedo A Jr, Srougi M and Ortiz V. Topical treatment for phimosis: time span and other factors behind treatment effectiveness. J Pediatr Urol. 2006 Aug;2(4):380-5.

22 Kuehhas FE, Miernik A, Sevcenco S, Tosev G, Weibl P, Schoenthaler M and Lassmann J. Predictive power of objectivation of phimosis grade on outcomes of topical 0.1% betamethasone treatment of phimosis. Urology. 2012 Aug;80(2):412-6.

23 TGA document https://www.ebs.tga.gov.au/servlet/xmlmillr6?dbid=ebs%2FPublicHTML%2FpdfStore.nsf&docid=E111CC0DDF687F4DCA2577DD000337FC&agid=%28PrintDetailsPublic%29&actionid=1

24 Srivastava A, Tepole AB and Hui C-Y. Skin stretching by a balloon tissue expander: interplay between contact mechanics and skin growth. Extreme Mechanics Letters. 2016;(9):175-187

25 Case Studies - On File with Manufacturer of Novoglan Product

26 Chittaranjan Andrade The Limitations of Online Surveys Indian J Psychol Med. 2020 Nov; 42(6): 575–576

27 On File with Manufacturer of Novoglan Product