Countering Contraceptive Controversies in the Media

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Declaration of Interest

- I've provided expert opinion and developed and delivered educational material for MSD, Bayer, Pfizer and Teva (who market the contraceptive preparations referred to in this presentation)
- I have in the past received support for conference attendance from MSD and Bayer

ABC- Spotlight on LARCs

- On the 11th December 2017 the ABC ran an article on the side-effects of LARCs on both their free-to-air and web platforms
- Their key points were that:
  - These products have grown in popularity in Australia
  - As COCPs go off-patent pharmaceutical companies have been waging massive marketing campaigns to promote these devices
  - Some women claim the impact on their mental health meant they have had to take anti-anxiety medication for the first time in their lives
  - TGA reporting data of adverse events (around 1%) was being ignored or downplayed

Personal Testimony- Ms Suzie Short

- Contraceptive implant inserted postpartum
- Vaginal bleeding for 7 months
- So lethargic her care of her infant child affected
- Despite the removal of the device she remains on antidepressants many years later and resents the impact on her ability to parent effectively
- Ms Short also ascribes her chronic abdominal pain to her use of the implant- '-all of my abdominal organs are fusing to my abdominal wall'

Personal Testimony- Ms Jane Morgan-Harry

- Mirena inserted following a miscarriage
- Problems with bleeding, headaches, sweats, the shakes, nausea -pretty much 24 hours a day
- Found difficulty convincing her clinicians that her symptoms were due to her Mirena
- Her period now lasts for two weeks each month but has been told she will have to wait more than a year to have the device removed in a public hospital
- The impact on her mental health has meant she had to take anti-anxiety medication for the first time in her life

Listening in on Social Media

Sandy- *"My 26-year-old daughter was one of those people who suffered terrible side-effects from an Implanon implant. Soon after having the implant, she found herself needing to take anti-anxiety medication and anti-depressants…. She made a complete recovery after removal of the implant but the damage had been done, and a vulnerability evidently remained, until she tragically and suddenly suicided some time later. I have had 3 mothers talk to me about similar situations with their daughters, who thankfully have had their Implanon removed in time.*

Lara- *"I had a Mirena put in after baby no.3 and 2 weeks later woke up with the whole right side of my body quite numb and weak. I then developed vertigo, nausea, eyesight went poor, had heart palpitations, cold sweats in the middle of the night, panic attacks and weight loss. I felt so weak I couldn't even carry my new baby, walk up the stairs or even brush my hair…..All I wanted to do was crawl in a hole and sleep. I literally thought I was dying it was that horrible. So then I started researching... And kept digging till I came across all the other women with problems and then it all made sense. I had the Mirena removed and I have gradually improved year by year."*

The Power of Personal Testimony- Beware the Anecdote

- Social Media (…and the ubiquitous commentary on media) allows for unmediated validation and amplification of the personal anecdote
- Journalists know that personal testimony engages the audiences, cultivates identification and emotional investment and enlivens dry research-based information
- The selection of which exemplars to use in a story tends to be guided by the subjective sentiment of the journalist/presenter
- Some journalistic guidelines have made recommendations on this point, such as:
  - When case studies are used they should be broadly consistent with the scientific evidence[1]
  - Understand that lay narratives may be problematic because they heighten emotionality and may displace the scientific message[2,3]

1. Vercellesi L et al. Health Education Journal 2010; 69(1):48–62
2. Boyce T. Journalism Studies 2006; 7(6): 889–906.
3. MacDonald SP. Written Communication 2005; 22(3): 275–97

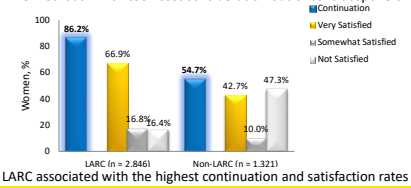
And the Result?

- Anecdotally patients at Family Planning Clinics and Hospital OPDs cancelled appointments for LARC in the week following the program
- The ABC received 17 complaints about the story, including a petition from health professionals and organisations. These have been referred to their independent complaints handling body
- RANZCOG[1] "The body of evidence in favour of the use of long-acting contraceptive methods is so strong that governments in the United States and the United Kingdom as well as numerous professional organisations across the world, including the World Health Organization, have recommended greater availability of LARC. The article from the ABC does a great disservice to women by presenting an unbalanced approach that is not based on facts and is contrary to the opinion of world leaders in this field."
- In fact the ABC report was contrary to most accepted evidence and clinical experience….

1. https://www.ranzcog.edu.au/news/RANZCOG-strongly-supports-long-acting-contraceptiv December 2017

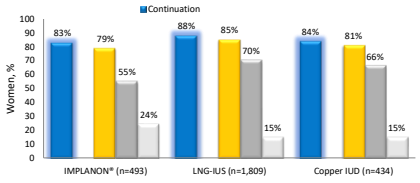
LARC vs non-LARC: 12-month Continuation and Satisfaction[1]

- The CHOICE Project was an independently funded (the Susan Buffet Foundation) project in St Louis in the US which allowed women access to LARC methods which took cost consideration out of contraceptive choice



- LARC associated with the highest continuation and satisfaction rates at 12/12

LARC: 12-month Continuation and Satisfaction[1]



- The difference in 12-month continuation rates between IUDs and IMPLANON was not statistically significant

Effectiveness of LARCs[1]

- Practical efficacy:
  - Non-LARCS- 95.55%
  - LARCs- 99.73%
- Women who used non-LARCs were **20 times more likely to have an unintended pregnancy** than those who used LARCs (Adjusted Hazard Ratio 21.8; 95% CI, 13.7 to 34.9)
- Women less than 21 years of age who were using non-LARC methods had **almost twice the risk of unintended pregnancy** as older women (Adjusted Hazard Ratio 1.9; 95% CI, 1.2 to 2.8)

Contraception Stories in the Media

- A Case of 'Boom and Bust'-new contraceptives are considered newsworthy but problems even more so
- Most women using contraceptives are young and healthy and adverse outcomes are perhaps 'more tragic' in such a group
- There are less 'specialist' health journalists these days and those reporting have obstacles to overcome- such as:
  - 'Hype' in science is on the rise
  - Wading through evidence is expensive, difficult tedious and time-consuming
  - There is not only pressure to get stories correct and on deadline but to produce hits – particularly online
  - In the age of 'false news' there are some who believe that getting it wrong is not really an issue because all will be forgotten in 24 hours

Contraceptive Scares from the Past


THE SAD LEGACY OF THE DALKON SHIELD

- Dalkon Shield introduced in US in 1969
- Polyfilament strings of this device were said to increase the risk of PID in users and several US studies (1976-1982)showed an increased risk of PID and septic abortion in Dalkon users[1]
- Millions paid in compensation and damages
- Device was withdrawn from US market in 1974 and the manufacturer filed for bankruptcy in 1985
- BUT a 1984 British study indicated no difference in PID incidence between the Dalkon Shield and 3 other IUDs fitted in 13,349 UK women from 1971-1978[2]

1. *CDC MMWR. Elevated Risk of Pelvic Inflammatory Disease among Women Using the Dalkon Shield May 6 1983; 32(17):221-222*
2. *Snowden R, Pearson B. BMJ 1984; 228: 1570-1573*

The Consequences

- Litigation extended to other IUDs
- From 1974 to 1986 no IUDs available in US
- By late 1980s 40% of US O&Gs were not recommending the IUD to **anyone**, citing legal liability as the major reason[1]
- Dramatic reduction in the use of IUDs in the US
  - 7% in late 1970s but by late 1980s, less than 2%[2]
  - Only in 2005 did FDA declare IUDs safe for nullips
  - Back to 7% in 2013[3]
- Impact on other countries variable[4]
  - Less impact in Europe and Scandinavia
  - In 2010 less than 2% of Australian women were using an IUD for contraception[5]

1. *Koelker CH et al. West J Med 1990; 153(3):279-282 2. Hubacher D et al. Contraception 2004; 69: 437-446*
3. *http://www.huffingtonpost.com.au/entry/iud-birth-control_n_8738234 4. Graph of IUD use from Sonfield A. Popularity Disparity: Attitudes About the IUD in Europe and the United States. Guttmacher Policy Review,Fall 2007, Volume 10, Number 4 5. Gray E, McDonald P. J Biosoc Sci 2010; 42(1):43-57*

Mirena® in the Medicolegal Spotlight

Rare Complications	Side-effects	Medically Implausible Claims
Uterine perforation	Amenorrhoea	'Migration' of the device after insertion
Embedding of the device in the uterine wall	Irregular bleeding	Vaginal erosion
Expulsion of the device	Pelvic Pain	Infertility
Pelvic Infection	Breast tenderness	Birth defects
Pregnancy	Ovarian Cysts	Vaginal scarring
Ectopic Pregnancy	Vaginitis	Life threatening infections
		Hysterectomy
		Death
		Various Malignancies

1. Table adopted from Danvers A et al. Lawsuits against Mirena: potential impact on Public Health. Contraception 2014 Jun;89(6):489-92

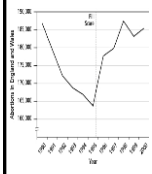
- Mass solicitation of US Women for side-effects/problems attributable to Mirena®- Nearly 2000 women joined various class actions
- Manufacturer and inserters accused of failing to inform women of these problems prior to insertion
- Range from acknowledged side-effects to the biologically implausible

Why should Women and their Health Providers be Concerned?

- IUDs have only just recovered from the negative perceptions of the past[1]
- Potential decrease in the use of a contraceptive method generally acknowledged as safer, highly effective and with secondary benefits[1]
- Use of less effective methods may increase risk of unintended pregnancy[1]
- Potential adverse impact on product availability and further contraceptive research, development and innovation[1]
- In October 2017 the New York Court of Appeals found against the 326 plaintiffs in the first Mirena case -on the basis of failing to prove causation for secondary perforation[2]
- Only 1700 plaintiffs to go and other suits continue…..

1. *Danvers A et al. Lawsuits against Mirena: potential impact on Public Health. Contraception 2014 Jun;89(6):489-92*
2. *https://hub.wolterskluwer.com/news/products-liability-law-daily/failure-to-prove-causation-ends-mirena-iud-litigation-against-bayer/41289/*

The 1995 Pill Scare



- In October 1995 warning issued by the British Commission on Safety of Medicines, on the basis of 3 unpublished studies[1,2,3] that there was an increased risk of VTE in women using OCPs containing third generation progestogens (OR from 1.5 to 2.3)
- Led to massive media coverage, brand switching and 12% of those on 3rd generation COCPs in the UK discontinued Pill altogether[1]
- 8% increase in TOPS in the UK over the following 12 months (13,000 additional abortions)[2]
- In same year deliveries increased by 20-25%[3]
- **No** reduction in VTE rates in the UK[4] or anywhere else in Europe[5]
- The 1995 studies were consistent in their findings-but consistently weak and findings more likely to be explained by bias than a causal relationship[5]

1. Hope S. Lancet 1996; 312: 576 2. Furedi A. Human Reproduction Update 1999; 5: (6) 621-626 3. Mills A. Human Reprod 1997; 12(12) : 2595-25984. Farmer RDT et al. BMJ 2000; 321(7259):477–479 5. Spitzer WO. Human Reproduction 1997; 12(11):2347-2357

And the VTE Controversy Re-emerges

- From 2007-2011 four retrospective case-controlled studies indicated risk of clotting was increased 2-3 times in patients taking 3rd gen progestogens compared with 1st or 2nd[1-4]
- BUT a number of other large studies (controlled prospective, cohort, case control) have shown no difference in blood clotting rates between older and newer COCPs[5-9]

1. van Hylckama Vlieg A et al. BMJ 2009;339:b2921 2.Lidegaard O et al. BMJ 2009;339:b2890 3. Jick SS et al. BMJ 2011; 340:d2151 4. Parkin L et al.BMJ2011;340:d2139 5. Dinger JC et al. Contraception 2007; 75: 344-354 6. Dinger J et al. Contraception 2014; 89(4): 253-263 7. Heinemann LA et al. Contraception 2010; 81(5):401-407 8. Seeger JD et al. Obstets Gyne 2007; 110:587-593 9.Dinger J et al. J Fam Plan Reprod Health Care 2010; 36:123-129

Still a Controversy or Media and Medicolegal Fait Accompli?

- Third generation Pills/Patches/Rings in USA must now carry warning of 2-3x risk of clotting
- 23 deaths ascribed to Yaz/Yasmin® use from 2007-2013 in Canada-most within 3/12 of initiation
  - Canadian Drug Regulatory Body issued warning
  - Large class action now in train
- In Australia:
  - In 2011 the TGA in Australia posted an advisory for drospirenone-containing Pills but did not restrict their use
  - Media attention from mid 2013 with investigative pieces making the case for an increased risk of VTE for those on Yaz/Yasmin®
  - In 2015 it was reported that 1000 Australian women had expressed interest in joining class action against the manufacturer[1]
  - The ABC journalist I contacted cited a number of Australian pieces on the increased risk of VTE on Yaz/Yasmin® as an example of

1. https://www.abc.net.au/news/2015-10-09/forces-for-class-action-against-contraceptive-manufacturer

Listening in……

Jacqui- *"At 25, I developed a blood clot in my leg. The haematologist ran tests and the only reason they could find was the Pill I was taking - Yasmin. Five years later I developed another clot in the same leg during my first pregnancy. They told me the first clot increased my chance of developing clots in the future. I do not have any clotting disorders or family history. I am now on injections once a day until I have finished having children. I really hope Yasmin is taken off the market, so there is less risk to other people."*

Lauren- *"I was prescribed Diane-35 ED when I asked my doctor for a contraceptive that would also help clear up my skin. Six months later I was rushed to hospital with clots. Apparently my blood is thicker than average and they should have done more testing before they just handed it over. Now I have to deal with that for the rest of my life. We had to go through IVF for my kids, and now I don't know if I should try for another pregnancy."*

Which brings us to Cyproterone Acetate Pills…..

- Indicated for androgenic symptoms with secondary contraceptive effects-it should not be used primarily for contraception and all peak bodies suggest that its continued use should be regularly evaluated by the treating clinician- particularly if risks accumulate
- In January 2013, the French Medicines Agency announced that it was deregistering CPA pills following the deaths of 4 women
- In May 2013, the European Medicines Agency concluded that the benefits of CPA Pills outweighed the risks- provided measures were taken to minimise the risk of VTE
- In July 2013 the European Union ordered France to lift the ban and they were reintroduced into the French market

And in Australia

- Federal MP Julian Hill is demanding the TGA either ban or impose tougher regulations on CPA Pills and that they only be prescribed after mandatory thrombophilia testing. Why?
  - In 2016 his daughter Elanor was diagnosed with a VTE after she firstly flew to Spain and then on to Sri Lanka. She was later found to be a Leiden V carrier[1]
  - She was commenced on a CPA Pill 3 weeks before her flight when diagnosed with PCOS[1]
  - Elanor admits that chat-rooms indicate that women specifically request CPA Pills specifically to improve their skin[2] but states she would never have taken this Pill had she been aware of the risk
  - She also regrets that her use of a CPA Pill has eliminated her future use of other COCPs and that her travel insurance is now a lot more expensive[3]

1. http://junkee.com/julian-hill-ban-diane-35/127936
2. https://www.4bc.com.au/contraceptive-pill-almost-kills-an-mps-daughter/
3. http://www.abc.net.au/triplej/programs/hack/blood-clot-because-of-pill-nearly-killed-daughter/9229256

A Clinical Aside….To Screen or not to Screen

- Having a first degree relative with a VTE under age 45 is a UKMEC3 for combined contraception[1]
  - A positive screen makes combined contraception UKMEC4
  - **But** a negative thrombophilia screen does not negate the risk of VTE- 50% of those with a proven VTE screen negative
  - The same thrombophilic disorder can have very different clinical penetrance within families
- Having a known Leiden V mutation can increase the risk of VTE on combined contraception 20-30 fold BUT:[2]
  - Leiden V mutation is found in up to 10% of Caucasians
  - The actual risk of VTE in carriers is still small-0.5% per annum
  - Most women with Leiden V will never have a VTE even after many years use of combined contraceptives
  - 10,000 women would have to be screened and combined contraception withheld in 500 otherwise healthy FVL heterozygotes to prevent one episode of VTE
  - Since death is even rarer (1-2% of VTEs annually) 92,000 women would have to be screened to prevent one death
- FSRH and other peak bodies state that 'a thrombophilia screen is **not** recommended routinely before prescribing combined contraceptives'[1]

1. file:///C:/Users/z3141678/Downloads/evaguidecombinedhormonalcontraception.pdf
2. Merriman L et al. Postgrad Med J 2006; 82(973):699-704

And back to Professor Lidegaard……

- Professor Øjvind Lidegaard is an epidemiologist at the University of Copenhagen. His group uses Denmark's impressive health database to look for associations between contraceptive use and outcomes-"The Danish Sex Hormone Register Study." Findings from this group have included:
  - Increased VTE risk on newer progestogens[1,2]
  - Increased VTE risk with the vaginal ring[3]
  - Decreased VTE and stroke risk in Mirena and Implant users (!)[3]
  - Increased risk of depression and antidepressant use in those on contraception- COCP(RR 1.23),Ring 1.6, Mirena 1.4[4]
  - Risk of depression amplified in adolescent users of contraception-1.8[4]
  - An increased risk of suicide in those on hormonal contraception- COCP 1.9, Ring 2.58[5]
- Absolute risk in all studies is small-but journalists almost always report relative risks
- Most of these published studies, and the interviews after, add the rider that they prove only an association and not causation and that further studies are required

1. Lidegaard O et al. BMJ 2009;339:b2890 2. Lidegaard O et al. BMJ 2011;343:d6423 3. Lidegaard O et al BMJ 2012;344:e2990
4. Skovlund CW et al. JAMA Psychatry. 2016;73(11):1154-1162 5. Skovlund CW et al. https://doi.org/10.1136/bmjopen-2017-019616

'Uncritical Reverence'

- Journalists are usually inherently sceptical of claims being made by government, industry and those with potential conflicts of interest. Yet with academia a less critical approach is often adopted
- Most universities have limited funds and large scale RCTs are rare
- Data-base studies are academic catnip since:
  - They are cheap to conduct-and are a gift that just keeps on giving in terms of potential data
  - You can put a whole team of postdoctoral students on to them and publish multiple papers on which everyone gets their name
  - You don't have to prove a thing and in fact if you have a contrary finding next year that's a bonus!
  - Any controversial findings will increase citations, interest factors and media attention

What are the Consequences of Poor Health Reporting?

- Media is an important source of health information- in one US survey 63% got their health-care information from cable TV news programs and 55% from broadcast news programs[1]
- The worried-well become concerned- driving people to unnecessary consultations and to demand unproven therapies
- Some may be wary of accessing treatment which may benefit them
- Some consumers will recognise the inconsistencies in such reporting and reject appropriate health information
- Clinicians must spend time debunking incorrect media information
- Clinicians, though unnamed, may be pilloried in the media without any ethical means of explanation or rebuttal
- The problem is that it is easier to scare people than 'unscare' them

1.Henry J, Kaiser Family Foundation: Kaiser health tracking poll—May 2010. [http://www.kff.org/kaiserpolls/8075.cfm]

So what can we do about all this?

- Insist on responsible dissemination of research evidence and that press releases put what is reported into context
- Advocate for better training for health journalists in research methods
  - You don't need to be a scientist to think critically and ask good questions about research but health journalists should have a basic understanding of study design, research methods, and, very simply, the scientific method
- Demand balanced reporting-in time and credibility as well as content
- Don't let poor health reporting slide…
  - Researchers/clinicians should hold media outlets that fail to put new findings in context or ignore available evidence to account by notifying reporters or editors when they spot shortcomings. The next step is simply to refuse to engage with repeat offenders
- More external independent commentary on the integrity of health stories such as https://www.healthnewsreview.org/
  - Around 70% of news articles reviewed by this site received unsatisfactory scores[1]

1. https://bmcmedinformdecismak.biomedcentral.com/articles/10.1186/1472-6947-13-53-S3

And a Last Gratuitous Piece of Advice..

- If a patient tells you she wants her implant or Mirena removed- take it out!

Thanks for listening!