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Infant male circumcision: An evidence-based policy statement

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ABSTRACT

Here we review the international evidence for benefits and risks of infant male circumcision (MC) and use this to develop an evidence-based policy statement for a developed nation setting, focusing on Australia. Evidence from good quality studies that include meta-analyses and randomized controlled trials showed that MC provides strong protection against: urinary tract infections and, in infancy, renal parenchymal disease; phimosis; paraphimosis; balanoposthitis; foreskin tearing; some heterosexually transmitted infections including HPV, HSV-2, trichomonas, HIV, and genital ulcer disease; thrush; inferior hygiene; penile cancer and possibly prostate cancer. In women, circumcision of the male partner protects against HPV, HSV-2, cervical cancer, bacterial vaginosis, and possibly Chlamydia. MC has no adverse effect on sexual function, sensitivity, penile sensation or satisfaction and may enhance the male sexual experience. Adverse effects are uncommon (<1%), and virtually all are minor and easily treated. For maximum benefits, safety, convenience and cost savings, MC should be performed in infancy and with local anesthesia. A risk-benefit analysis shows benefits exceed risks by a large margin. Over their lifetime up to half of uncircumcised males will suffer a medical condition as a result of retaining their foreskin. The ethics of infant MC and childhood vaccination are comparable. Our analysis finds MC is beneficial, safe and cost-effective, and should optimally be performed in infancy. In the interests of public health and individual wellbeing, adequate parental education, and steps to facilitate access and affordability should be encouraged in developed countries.

Keywords: Male Circumcision; Public Health; Infant Infections; Sexually Transmitted Infections; Cervical Cancer

1. INTRODUCTION

The Circumcision Foundation of Australia was formed in 2010 to provide education, clinical training and commentary on male circumcision (MC) [1]. At present there is an absence of *evidence-based* policy on this topic in developed countries such as Australia. This, despite the increase in recent years in the quality and quantity of evidence in support of medical MC as a result of numerous studies that have included wide-ranging findings from large randomized controlled trials (RCTs) and meta-analyses. Calls have been made in Australia [2,3], the USA [4,5],

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and the UK [6] for infant MC to be encouraged because of the considerable benefits it confers to public health and individual wellbeing [7]. Until the 1970s infant MC was routine in for Australia, but the rate may now be less than 20%, despite increases in the two most populous states over the past decade [8]. This further highlights the need for evidence-based policy. Here we provide a comprehensive up-to-date review of the diversity of benefits and the risks of infant MC in formulation of such a policy.

2. METHODS

A detailed examination was conducted of references from the first author's lifetime collection, most of which had been accumulated over the past two decades from weekly alerts based on the key-word "circumcision" from NCBI PubMed over the past 5 years and Current Contents prior to that. We then evaluated the quality of the evidence using the Scottish Intercollegiate Guidelines Network (SIGN) grading system for evidence-based guidelines [9], which ranges from 1++ (highest) to 4 (lowest).

3. RESULTS AND DISCUSSION

3.1. Urinary Tract Infection (UTI)

The highest prevalence and greatest severity of UTIs is in the first 6 months of life [10,11]. UTIs are common [12] and can lead to significant morbidity [13]. Prevalence is 1% - 4% in uncircumcised boys, and 0.1% - 0.2% in circumcised boys [11,14-18]. The protective effect of MC was confirmed by a RCT, which noted a 96% decrease in UTI after treatment by MC at age 6 months [19]. Cumulative prevalence to age 5 was 6% in uncircumcised boys in Western Sydney, with only 2 circumcised boys experiencing a UTI [20]. Although prevalence decreases after infancy [21], there is "no evidence that the patient's age modified the protective effect of circumcision status on the development of UTI" [20]. Cumulative prevalence to age 16 was 3.6% in uncircumcised boys in a UK study [22]. In US men, circumcision reduced UTI prevalence by 5.6 fold [23], and over the lifetime cumulative incidence of UTI in the uncircumcised is 1 in 4 [24].

UTI may lead to an acute febrile condition and significant symptoms such as severe pain. Often the cause of the fever is undiagnosed. If the boy is uncircumcised a UTI should be suspected. Boys presenting with fever have UTI as the cause in over 20% of cases if uncircumcised, but only 2% if circumcised [25,26]. In febrile infants bacteriuria is seen in 36% of uncircumcised boys, indicating that a UTI as the likely cause of fever, compared with only 1.6% of circumcised boys, a 23-fold difference [27]. The American Academy of Pediatrics Subcommittee on Urinary Tract Infections recommends a urine culture for any child under 2 with unexplained fever. Most boys are hospitalized and given parenteral antibiotics.

Acute pyelonephritis is seen in 90% of infants with a febrile UTI [28], 34% - 86% of whom exhibit renal parenchymal defects [21,29], and 36% - 52% will show renal scarring [28]. This exposes them to serious, life-threatening conditions later in life [30], including end-stage renal disease in 10% [31].

Recurrence of UTI occurs in 35% of UTI cases in infant males. Urinary tract abnormalities increase the risk of recurrent UTI, but 10% of UTIs occur in the absence of a urinary tract abnormality [20], nonretractile foreskin and acute pyelonephritis being the biggest risk factors for recurrence [32]. MC moreover protects against recurrence [33]. In 36% of boys acute pyelonephritis is seen in the absence of vesicoureteric reflux (VUR) [32]. Pyelonephritis can lead to renal scarring, and most children who develop renal scarring do not have VUR [34]. Parenchymal infection and inflammation, rather than VUR, is a prerequisite for renal scarring [34]. Advice that MC only be recommended in boys with recurrent UTI or VUR has been criticized as flawed [35].

Because UTIs are often associated with long-term morbidity and potential mortality [12], prevention by circumcision is recommended.

3.2. Hygiene

A circumcised penis is generally easier to clean. Even if the male or his parents routinely retract the foreskin to clean under it, pathogenic bacteria [36] quickly return [37,38]. Better hygiene is often stated as the main reason why Australian parents have wanted their baby boy circumcised [39]. Penile hygiene has been found to be inferior in uncircumcised schoolboys [37,40] and London men [41], especially those with long foreskins [42]. Starting in adolescence, smegma accumulates under all foreskins that are not easily retractable. Yeast and some bacteria, notably *Mycobacterium smegmatis*, cause smegma to have an offensive odour [43,44].

3.3. Inflammatory Dermatoses

Inflammation of the penis, in the form of balanitis, posthitis and balanoposthitis, is common in uncircumcised males [3]. A frequent cause is *Candida* spp. infection [45]. A meta-analysis of 12 studies found that MC reduced balanitis by 3-fold (OR 0.32; 95% CI 0.20 - 0.51) (J.H. Waskett, unpublished). In children, balanitis affected 5.9% of uncircumcised boys in one survey [46] and 14% in another [47]. A cross-sectional study of randomly selected dermatology patients found balanitis in 13% of uncircumcised, but only 2.3% of circumcised men [48]. Treatment of balanitis was the reason why 29% of those men had to be circumcised.

3.4. Phimosis and Paraphimosis

Phimosis is the narrowing of the foreskin orifice, some-

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times to a pinpoint, so as to prevent normal retraction of the foreskin over the glans [49]. While this state is normal under age 3, if still present by age 6 it is regarded as a problem. Clinical observations and survey data reveal prevalence of phimosis in youths and men is 8% - 14% (see reviews [3,7]). Phimosis may arise from physiological adhesion of the foreskin to the glans, or from fibrous adhesions due to acquired pathology such as balanitis xerotica obliterans (BXO) [50] that causes secondary cicatrization of the foreskin orifice. BXO-induced phimosis presents most commonly at age 8 - 10 years [50]. Once thought to be rare and a disorder presenting in adulthood, BXO is now regarded as common in boys, in whom treatment by MC is advised to prevent the complications that occur later in life [51]. Of 13 studies, BXO was the cause of phimosis in 25% of cases [7]. Although treatment by a month or so of continued application of steroid creams can be effective in the short-term, a RCT showed that in the long-term recurrence of phimosis is frequent, requiring retreatment or circumcision [52].

Paraphimosis refers to an inability to return the foreskin after retraction over the glans. This painful condition causes a severe diminution of blood flow to the glans, and its occurrence represents a medical emergency since gangrene of the distal penis can occur [49].

3.5. Sexually Transmitted Infections

Male circumcision protects against many, but not all, sexually transmitted infections (STIs) [53]. In the case of syphilis, genital herpes (HSV-2) and chancroid, a meta-analysis of 26 studies, including 2 from Australia, found lower prevalence in circumcised men [54]. For oncogenic HPV, a recent meta-analysis of 23 studies, including 10 from the USA, found overall prevalence of DNA for such viral types to be 41% lower overall in circumcised men, but 53% lower on the glans/corona and 65% lower in the urethra [55]. Longitudinal studies in two New Zealand populations found self-reported lifetime STIs was higher in uncircumcised men in one [56], but no different in another [57]. The latter group found no difference in HSV-2 [58] or HPV [59] seroprevalence. Seroprevalence indicates previous exposure, rather than incident infection, which is higher in uncircumcised men possibly because circumcised men clear HPV faster [55,60-62]. Secondary analyses from high quality RCTs support the protection afforded by MC against incident HSV-2 [63,64] and HPV [61,65-70]. This included showing 97% protection against HPV-related flat penile lesions [71]. A US study saw 64% lower HSV-1 seroprevalence in circumcised men [72]. MC also protected against genital ulcer disease (GUD) [73,74], including in HSV-2 seronegative men in one trial [75]. MC does not protect against sexually transmitted urethritis in men [76].

A strong case can be made for infant MC in developed countries in reducing some STIs, because: 1) There is an epidemic of oncogenic HPV and HSV-2, with seroprevalence in young men of 25% [59] and 8% [58,77] for each respective virus; 2) In the case of Australia, MC prevalence is decreasing as males not circumcised in infancy continue to enter sexually active age groups [78]; 3) The average number of sexual partners and STI prevalence is rising [79], but condom use was not in senior high school [79] and high-risk [80] adolescents [79]; 4) Condoms, while helpful, vary in efficacy against different STIs, being only partially protective against HPV [59,81-83] and HSV-2 [84], and are not used at all or are used only sporadically by many people [57,85-89]. Condoms have to be applied each time, and are therefore often not in place during sex, whereas MC is always present; 5) Infancy is the best time to perform MC as it ensures the male is already protected by the time he becomes sexually active.

3.6. HIV

Male circumcision affords over 60% protection against HIV, as confirmed by 3 large RCTs [74,90,91] and later endorsed by a Cochrane review [92]. Meta-analyses of observational studies found protection to be similar [93-95] or stronger [96] than in the RCTs. The epidemiological findings are supported by biological evidence [97]. As pointed out in one of the meta-analyses [95], MC satisfies 6 of the 9 criteria of causality outlined by Sir A.B. Hill [98]—strength of association, consistency, temporality, coherence, biological plausibility, and experiment. Follow-up data indicate an ongoing increase in the protective effect of MC [99-101] to 73% after 5 years [101]. This means that MC is as effective in HIV prevention as vaccines against influenza [102,103]. So "early stopping [of the RCTs] may have underestimated the effect [of MC]" [93]. Acceptance by the WHO and UNAIDS [104] has been followed by the large-scale implementation of MC in sub-Saharan Africa, early data revealing a protective effect of 76% [105].

Although no data exist in Australia, the protective effect of MC against HIV infection from heterosexual contact is likely to be just as great as in the USA [106-108]. While such infections were negligible in the 1980s, this mode was responsible for 10% of new HIV diagnoses in the USA in 2010 [109] and 23% (1185 cases) in Australia in 2005-2010 compared with 841 (20%) in 2000-2004 [110]. After excluding infections acquired in a high prevalence country, there were 527 HIV cases from heterosexual contact in 2000-2004, rising to 703 in 2005-2009, a 33% increase (38% in men and 28% in women) [110]. The highest proportion (31%) was in Australian-born individuals. Such trends have led to calls for infant MC to be encouraged strongly in Australia [2]. Similarly, the Centers for Disease Control and Prevention (CDC) has affirmed the value of MC [4,111], finding infant MC to be cost-saving for HIV prevention in the USA [112].

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For men who have sex with men (MSM), a Sydney study found MC had an 89% protective effect in the 1 in 3 men who were insertive-only [113]. Such protection is supported by a meta-analysis of 18 studies [114] and a Cochrane review [115]. Circumcision of insertive-only MSM appeared, moreover, cost-effective for HIV prevention in Australia [116].

The cost of MC is a fraction of anti-retroviral treatment, the effectiveness of which requires strict compliance. Moreover, HIV prevention should be the primary focus of national policy. A cure, microbicide or a vaccine still appear to be a long way off [117].

3.7. Cervical Cancer and STIs in Women

Over 99% of cervical cancers are caused by oncogenic HPV types [118] that are an epidemic worldwide, including Australia. A large multinational study found cervical cancer in monogamous women whose male partner was high-risk (had had six or more partners or was aged <17 at first sexual intercourse) to be 4 times higher if the man was uncircumcised, and twice as high if he had an intermediate sexual behavior risk index [83]. These categories encompass most men in Australia and other developed countries. A meta-analysis of 14 studies, two performed in Australia, confirmed the ability of MC to protect against cervical cancer [119]. An inverse relation exists between MC and cervical cancer prevalence across 118 countries [120]. Secondary data from a RCT showed MC reduces HPV acquisition in the female partners by at least 28% [121].

Prophylactic vaccines against 2 of the over 15 types of oncogenic HPV are predicted to slowly reduce by half [122], but never eliminate, cervical cancer incidence over coming decades [123,124]. MC and vaccination should be regarded as synergistic for cervical cancer reduction. Vaccination of boys would have only limited benefits [123] and at present is not considered cost-effective [123-125].

HPV acquired during oral sex is an independent risk factor for some oropharyngeal cancers [126], which are rising in prevalence in the USA [127]. A study is needed of the MC status of the partner and such cancers.

MC also reduces by at least half the female partner's risk of HSV-2 [84,128,129], *Chlamydia trachomatis* [130], *Trichomonas vaginalis* [131], and bacterial vaginosis [131, 132]. Observational studies and secondary analyses of RCT data suggest transmission of HIV to women is 20% - 46% lower if their male partner is circumcised [133-135].

3.8. Penile Cancer and Prostate Cancer

Lifetime risk of penile cancer in an uncircumcised man is approximately 1 in 1000 in the USA [136]. MC greatly reduces the risk of penile cancer [137,138]. Meta-analyses have shown major risk factors to be phimosis (12-fold increase) [137], balanitis (4-fold) [137], smegma (3-fold) [137], and HPV (3 - 7 fold depending on type of squamous cell carcinoma) [139], all of which are more common in uncircumcised men [137]. Meta-analyses, that included studies from the USA, Australia and other countries, found MC halved the risk of oncogenic HPV infection [55,119,137]. Subsequent data from secondary analyses in the large HIV RCTs lends weight to these findings [61,65-70]. This includes demonstration in one of these of a 97% reduction in penile lesions caused by oncogenic HPV types [71]. One reason could be that circumcised men clear HPV infections more quickly, so reducing incident infection [55,60-62]. Particular attention should, however, be paid to the ~10% of uncircumcised men who have phimosis [3] as this is another major risk factor [137].

In the case of prostate cancer the evidence is mixed, yet sufficient data exist for a protective role that MC should be explored more extensively (see review [137]). If verified, MC could greatly reduce disease burden and associated costs [140].

3.9. Effect of MC on Sexual Function, Sensation and Satisfaction

Well conducted research studies have found no adverse effect of MC on penile sensitivity [141-144], sensation [145], sexual satisfaction [142,146], premature ejaculation [147], intravaginal ejaculatory latency time [148,149], and erectile function [78,142,150-152]. Such findings have now been supported by two large RCTs [153,154]. One of these found that MC improved sensation during sexual intercourse, leading to reports of better sex [154]. Two studies that found MC reduced risk of premature ejaculation was regarded by the men as a benefit [155,166]. A minority of studies has reported moderate adverse effects, but expert scrutiny [157-159] of these has revealed fundamental flaws that make the findings unreliable. There is some evidence that among 7 aspects of sexual function, for 6 there was no difference between men circumcised in infancy and those circumcised later, but for one, avoidance behavior, infant MC was more advantageous [160].

In the case of MSM, a study in Sydney found no differences in participation in insertive or receptive anal intercourse, difficulty in using condoms, or sexual problems such as loss of libido [161].

The female partners of men have found no adverse effect on their sexual experience after MC. A Mexican study found no change in sexual satisfaction, desire, pain during vaginal penetration or orgasm after their male partner had been circumcised [162]. In a RCT involving 455 women, 57% reported no change, while 40% reported an improvement in sexual satisfaction after circumcision of their male partner [163]. US studies have found that most women preferred the circumcised penis for sexual activity, hygiene and its appearance [164,165].

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3.10. Circumcision Techniques

Circumcision involves firstly freeing the foreskin that is lightly adherent to the glans and then, by freehand methods or assistance from a device, the removal of the foreskin. An array of instruments is available to improve accuracy and safety [166]. The devices differ for infants, older children and adults [166]. In Australia the Plastibell device is commonly used for infant circumcisions, whereas in the USA the Gomco clamp tends to be preferred. The Plastibell is affixed, a ligature is applied, and the residual, necrotic foreskin and ring fall off several days later. The Gomco clamp and Mogen clamp allow the circumcision to be completed at the time. When circumcision is performed in infancy the ability of the inner and outer foreskin layers to adhere to each other means sutures are rarely needed and the scar that results is virtually invisible [167].

3.11. Anesthesia

Anesthesia should always be used. A local anesthetic is preferred as general anesthetics present unnecessary risks, including neurotoxicity and death [168], and are unnecessary [169]. The best time is early in infancy when the infant is less mobile [169]. Topical lidocaine-based creams such as LMX4 [170], dorsal penile nerve block [171] using a portable ultrasound scanner as a guide [172], penile ring block [173,174], and other methods can be used. While pain can be almost completely eliminated by local anesthetics, neonates exhibit lower pain scores than older infants [175], their response to pain is less for vaginal than caesarean delivery [176], and early exposure to noxious or stressful stimuli decreases pain sensitivity and behavior in adult life [177,178]. For MC without anesthetic there may be some short-tem memory of pain [179], but no credible evidence has been produced in support of any longterm memory of pain experienced in infancy.

3.12. Complications

In infancy, surgical complications for large published series range from 0.2% to 0.6% [15,180-183]. Higher rates of 2% - 10% have been reported in much older and smaller studies [184-186]. A recent systematic review found a median frequency of complications for neonatal or infant MC of 1.5% compared to 6% for studies of medical MC of children aged one year or older [187]. In both infants and older boys severe complications were extremely rare [187]. In men, RCT data indicated complication rates of 1.7% - 3.8%, none of the events being severe [74,90,91,188]. At any age, complications are virtually all minor and immediately treatable, with a satisfactory outcome. The higher complication rate after infancy is another argument for MC soon after birth.

Dubious Internet advice to circumcised men with sexual problems on recreation of a (pseudo) foreskin can result in damage to the penis [189].

3.13. Ethical Considerations Regarding Neonatal Circumcision

Circumcision should be regarded as a minor medical procedure. To maximize medical benefits and minimize risks and costs, circumcision should be performed in infancy. Parental choice in this regard is consistent with the rationale behind vaccinations, another minor medical procedure also performed before the child is old enough to give consent [190,191]. The authors of one bioethical analysis concluded that MC is appropriate for parental discretion [191]. An alternative view, based on right to autonomy, is that circumcision should be delayed until the male can decide for himself [192,193]. Other bioethicists and legal commentators argue that in view of the risks of not circumcising, infant MC is a justifiable public health measure [194,195].

As discussed, UTIs are common in infancy, as is the damage they cause to the still-growing kidney. Infant MC provides immediate protection against other common pediatric conditions such as phimosis, paraphimosis and balanoposthitis. After evaluating all of the evidence it is apparent that infant MC has a very favorable benefit versus risk, especially considering the diversity of other benefits that accumulate through the boy's lifetime (**Table 1**). MC in infancy is safer, simpler, quicker, cheaper, more convenient, healing is faster and the cosmetic result is superior to MC later. Other bioethicists have argued that MC in some contexts is ethically imperative, as to do otherwise would risk human lives [194]. Complications are, moreover, more common in older males than for neonatal or infant circumcision. Delay places children at higher risk of conditions that could be largely avoided if they had been circumcised in infancy. Later circumcision is also unrealistic and impractical [196]. The argument that adolescents or men should make the decision defaults to almost none of the men choosing to be circumcised, even when they know that there are clear benefits and would like to be circumcised [197].

In this era of preventive medicine infant MC is a logical decision that parents should be encouraged to make. The ethics of infant MC and childhood vaccination are comparable. The right of parents to decide whether or not to have their sons circumcised must be respected.

4. CONCLUSION

The current scientific evidence is more than adequate to support a recommendation of MC in Australia and other developed countries as a low-risk, highly beneficial procedure that is best performed in infancy using a local anesthetic. Infant MC should appear on the check-list of decisions responsible parents need to make for their children

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Table 1. A comprehensive risk-benefit analysis of infant male circumcision.

Risks from not circumcising Condition	Level of evidence*	Fold increase	NNT†
Urinary tract infection (infants)	1++	10	50
Urinary tract infections (lifetime)	2+	5	4
Pyelonephritis (infants)	2+	10	100
-with concurrent bacteraemia	2+	20	1000
-childhood hypertension	2	–	1500
-end-stage renal disease (lifetime)	2	–	500
Candidiasis	2	2	10
Prostate cancer	2	1.5 - 2	6
Balanitis	2++	3	10
Phimosis	1++	infinite	10
High-risk HPV	1++	3	2
Genital herpes (HSV-2)	1+	1.3	5
Syphilis	1+	3	200
HIV infection	1++	3 - 8	1000
Penile cancer	1++	>20	1000
In female partner			
Cervical cancer	1++	4	–
Chlamydia	2+	4	–
HSV-2	2+	2	–
Bacterial vaginosis	1+	2	–

Thus risk in an uncircumcised male of developing a condition requiring medical attention over their lifetime = 1 in 2.

Risks associated with medical circumcision in infancy condition	Fold-increase	NNH
Local brusing at injection site if dorsal nerve block used	0.25**	4
Infection (local)	0.002	600
Infection (systemic)	0.0002	4000
Excessive bleeding	0.001	1000
Need for repeat surgery (if skin bridges or too little foreskin removed)	0.001	1000
Loss of penis	Close to zero	>1 million
Death	Close to zero	>1 million
Loss of penile sensitivity	0	>1 million

*As per Scottish Intercollegiate Guidelines Network (SIGN) grading system for evidence-based guidelines [9], which ranges from 1++ (highest) to 4 (lowest). Values shown are based on statistics for USA (for source data see review [7] and references cited in the present article). Abbreviations: †NNT, number needed to treat, *i.e.*, approximate number of males who need to be circumcised to prevent one case of each condition associated with lack of circumcision. ††NNH, number needed to harm, *i.e.*, approximate number of males that need to be circumcised to see one of each particular (mostly minor) adverse effect. **The minor bruising (from this method only) disappears naturally without any need for medical intervention, so is not included in overall calculation of easily-treatable risks.

Table 2. Some early childhood health interventions.

Breast-feeding
Immunization according to recommended vacciantion schedule against hepatitis B, rotavirus, whooping cough, measles, rubella, tetanus, mumps, polio, diphtheria, hemophilus influenzae type B, chickenpox
Circumcision if male, ideally in early infancy
Nutritional food for age according to recommendations
When placed in motor vehicle, safe, rear-facing baby capsule
Safe environment—stairs barricaded, dangerous object out of reach, etc.
Prevention of over-heating or cooling
Love, nurturing, education, exercise, etc.

(**Table 2**). The major factors discouraging infant MC are probably biased information often provided to young parents, a ban on performing infant MC in most public hospitals in Australia, withdrawal of Medicaid funding in a growing number of states in the USA [198,199], and in Australia a low Medicare rebate which makes infant MC unaffordable for low-income families. Each of these issues needs to be addressed by governments and health authorities. Further research on MC in Australia and other developed countries is to be encouraged.

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BJM was involved with the conception, information retrieval and writing of the initial draft of the manuscript. All other authors provided important input and suggestions for changes to the initial draft.

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