

REVIEW

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Exposing the Influence of Preceding Sexual Behavior in Younger Years toward Prostate Cancer Occurrence: Qualitative Mapping on Sexual Risk Factors

Naufal Nandita Firsty¹, Syah Mirsyah Warli^{2,3*}, Adrian Joshua Velaro⁴, Ginanda Putra Siregar^{2,3}, Dhirajaya Dharma Kadar^{2,3}, Fauriski Febrian Prapiska^{2,3}

Abstract

Introduction: Prostate cancer (PCa) is a multifactorial disease influenced by genetic, hormonal, and lifestyle factors, yet the impact of preceding sexual behaviors remains underexplored. Given the prostate's fundamental role in male sexual function, this study aims to qualitatively assess the relationship between ejaculation frequency (EF), first sexual activity (FSA), and lifetime sexual partner (SP) count with PCa occurrence in later life. **Materials & Methods:** A systematic literature review was conducted following PRISMA guidelines, with studies identified through MEDLINE, ScienceDirect, and ProQuest databases. Retrospective cohort and case-control studies published since 2000, examining PCa risk in relation to sexual behaviors in early adulthood (20s–40s), were included. Data extraction focused on EF, FSA, and SP count, and study quality was assessed using the Newcastle-Ottawa Scale. **Results:** A total of 10 studies with 6,601 PCa cases and 6,208 controls were analyzed. Higher EF from sexual intercourse (SI; ≥ 5 –12 times per month) was associated with a reduced PCa risk, whereas frequent masturbation (≥ 2 –7 times per week) showed a potential risk increase. The influence of FSA was inconsistent, with some studies linking earlier or later initiation to higher risk. A higher lifetime SP count (7–21 partners) was generally associated with increased PCa risk, likely due to sexually transmitted infections and chronic inflammation. **Conclusion:** Sexual behaviors in younger years may play a role in PCa development, with EF type, FSA, and SP count acting as potential risk modifiers. While high EF from SI may be protective, excessive masturbation and multiple partners could contribute to risk. Further prospective studies are needed to refine recommendations on sexual health and prostate cancer prevention.

Keywords: Ejaculation frequency- First sexual activity- Masturbation- Prostate cancer- Sexual behavior- Sexual partner

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Introduction

Understanding a multifactorial disease such as prostate cancer (PCa) requires a broad yet specific clinical perspective on its possible origin, considering numerous interplays of factors to the organ may eventually decide its cancerous growth [1, 2]. As an important sexual organ in males, the biological activity of the prostate is directly related to the individuals' sexual behaviors, as increased androgenic activity (e.g., elevated endogenous testosterone levels) may endorse higher prostatic cells turnover which theoretically increase the possibility of neoplasm transformation [3, 4]. According to the current report by GLOBOCAN in 2022, PCa is placed 2nd in term of annual total cases, unequivocally common in clinical practice, and eventually leading toward significant socioeconomic burden on both patients and stakeholders;

raising a need to identify and answer the ever-growing problem through risk factor analysis [5]. Though classical risk factors i.e., age, family history, race, or even genetic polymorphism has been numerous described in recent evidences, the impact of sexual behaviors toward PCa risk is often overlooked, albeit the organ's fundamental role in performing sexual activities and its related behavioral aspects should be investigated within greater scope of perspective.

The main idea of our study inquiries is predominantly based on a life-long modern society myth that requires actual fact-checking i.e., how the ejaculation frequency in males' younger years affect the risk of PCa diagnosis later? Although to date there is not any single and specific number of ejaculation rate per month that being considered "normal" in daily basis, it is theoretically sound to declare that altered ejaculation rate i.e., extremely frequent

¹Department of Urology, Faculty of Medicine, Universitas Indonesia - Cipto Mangunkusumo Hospital, Jakarta, Indonesia.

²Department of Urology, Faculty of Medicine, Universitas Sumatera Utara Hospital - Universitas Sumatera Utara, Medan, Indonesia.

³Division of Urology, Department of Surgery, Faculty of Medicine, Universitas Sumatera Utara - Haji Adam Malik General Hospital, Medan, Indonesia.

⁴General Practitioner, Djasamen Saragih Hospital, Pematangsiantar, Indonesia. *For Correspondence: warli@usu.ac.id

or nearly-sexual abstinence may eventually affect the PCa risk [6, 7]. Furthermore, other related aspects i.e., how early an individual experienced sexual activity and how many sexual partners does he have might, in fact, correspond to the overall prostatic activities, implying the need to assess the link between sexual behaviors and its consequence to the prostate well-being in older age [8]. For that reason, this study is aimed to qualitatively elaborate the influence of sexual behaviors in younger years toward subsequent PCa diagnosis, and how should we respond to the currently available investigation through a narrative- and partially-systematic approach.

Materials and Methods

Study design and literature searching

Our study adheres the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) protocol for its preparations, as it guided our intention to create a research question i.e., do preceding sexual behaviors during individuals' younger years may remarkably influences the PCa risk? The protocol of this review preparation is available in PROSPERO: International Prospective Register of Systematic Reviews under registered record ID of CRD420251002942 to ensure appraisable study blueprint [9].

To design is to be accurate, and by employing strategic keywords in Boolean term understanding, we sought to attain 'designated' literatures to be systematically analyzed further. The keywords straightforwardly revolved around "prostate cancer", "sexual behaviors", "masturbation", "sexual activity", and other sexual-related phrases that mostly falls on preceding sexual behaviors; as we conduct the literature searching on scientific databases e.g., MEDLINE, ScienceDirect, and ProQuest (studies identification only performed on its title-abstract searching to enhance the specificity of our search, each keyword is expanded based on MeSH system to amplify searching range). The literature searching was initially performed by 2 authors (N.N.F. and A.J.V.), with the results had been thoroughly discussed with other co-authors to verify the process, in which afterwards will be selected even further by employing eligibility criterion. The protocol of this review will be available on PROSPERO: International Prospectives Register of Systematic Review under the issue electronic ID of.

We strictly limit the literature eligibility to retrospective cohorts or case-controls, matched with our objective to investigate younger years (in respective populations' 20s to 40s) sexual behaviors, observation period as early as year 2000 (after new millennia and onwards), and performed on the 'current' PCa patients (unquestionably males) who underwent complete evaluation to be clinically and/or histopathological confirmed of having prostate malignancy (regardless the staging on diagnosis). The sexual behaviors aren't limited to frequency or intensity, but may as well be extended to the first sexual age (FSA) or even sexual partner (SP) counts and its orientation if possible (though its in-depth elaboration may be possible on the discussion section). Exclusion criterion was also applied as well i.e., literatures that were published in

languages other than English or Spanish, including other cancers or malignancies to be evaluated with preceding sexual behaviors, and unclear comparator groups (it is traditionally classified into high- and low- 'intensity' sexual behaviors, and subsequently compared). Therefore, the main idea of this review is rather straightforward, as it simply grounded on evaluating the influence of preceding sexual behaviors on the PCa occurrence in later life, as reviewed in retrospective 'formulation'.

Risk of Bias Assessment

To ensure the quality of each included studies, a total of 3 authors (N.N.F., A.J.V., and M.H.W.) performed a risk-of-bias (RoB) assessment by utilizing the Newcastle-Ottawa Scale (NOS) tool for retrospective cohorts and case-control studies. The discrepancies between authors will be resolved with the first author (S.M.W.) in a series of internal discussion to rigorously re-evaluate the qualities overall [10].

Data Extraction

From each eligible study, we attempted to recognize and 'extract' every study's identifier i.e., first author's last names and publication year. We also documented each study's location, observation period, population size, and age of the participants. Implementing systematic approach may be translated into collectively review the outcomes, as denoted by 3 major aspects in this study i.e., ejaculation frequency (EF; either resulted from sexual intercourse (SI) or masturbation-related), first sexual activity (FSA; similar to ejaculation frequency, could be interpreted as age of first coitus age or earliest age recalled of having a self-induced orgasm, and sexual partnership details (SP; total individuals count or possibly, sexual orientation). All findings on from the 'fitting' studies will be narratively extracted into a 'master table', with all P-values to represent its significance are a mandatory to be included as well. To unpack the cultural vs. biological impacts of the outcomes, we also performed a subgroup analysis based on the geographical location of the respective studies, hence we may acquire possible explanation on the observed influence of EF, FSA, or SP on the PCa risk based on the regional-based scoping analysis.

Results

We identified a total of 10 studies to be included in the final analysis, with 6,601 PCa cases will be systematically compared with 6,208 controls (non-PCa populations). The literature selection processes are presented in PRISMA flow diagram (Figure 1), as we only able to identify 10 eligible studies in this narrative systematic review. All of the studies were conducted no later than year 2000s to ensure similarity in modern sexual culture, and represented from different continents as well e.g., Canada and Mexico (North America); Spain, United Kingdom, and Turkey (Europe); Australia (Oceania), Taiwan (Asia), Iran (Middle-East), and Barbados (Caribbean). Considering all studies included male population mostly in their 50s to 60s, each respective populations' younger years should fall approximately in the 1970s era, partially

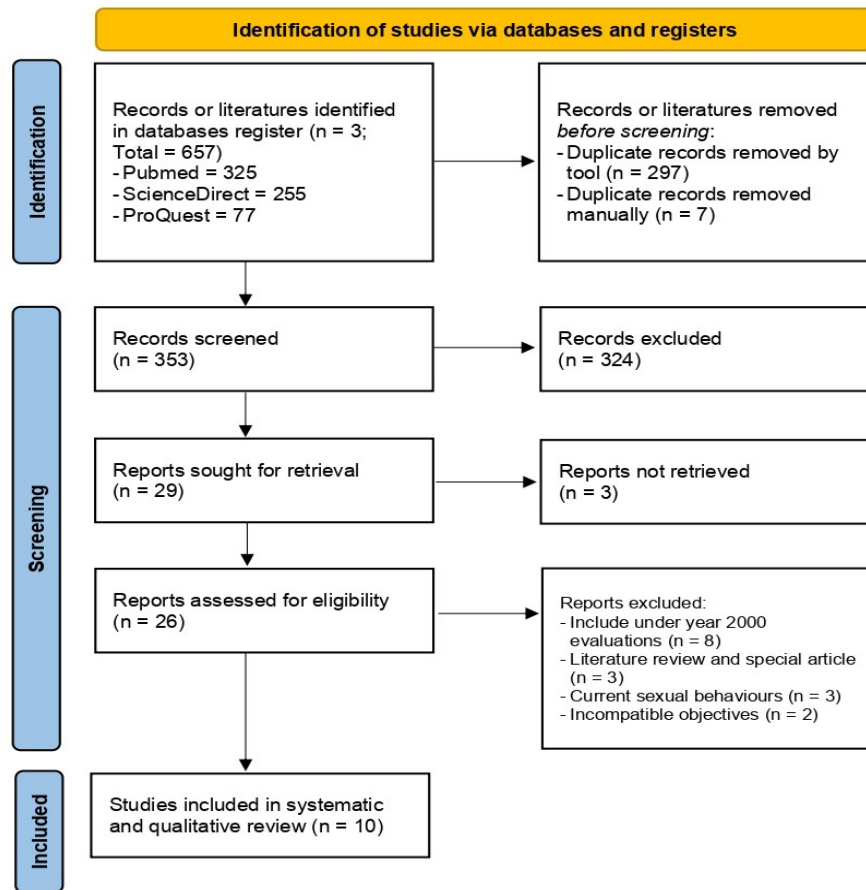


Figure 1. PRISMA Flow Diagram for Studies' Selection in This Study

portraying the sexual customs from pre-new millennia era. Further assessment on the studies' quality by NOS tool also demonstrated that all investigations are subjectively acceptable to illustrate sexual behaviors-related aspects to PCa occurrences.

A total of 3 major sexual behaviors-predictive factors for PCa occurrence in current ages were identified and subsequently described further in Table 1 i.e., ejaculation frequency (EF), first-sexual activity (FSA), and sexual partner (SP) count or details. To re-elaborate our findings, we also designed a 'visually-simplified' version of this systematic review in flowchart (Figure 2).

Ejaculation Frequency

As seen on both presentation tools, the impact of higher EF from sexual intercourse (SI) only isn't necessarily unpleasant, as at least 2 studies (Ahmadi et al. [11], (Iran) and Angeles-Garay et al. [12], (Mexico)) reported that EF >5-12 tpm and >2 tpw might, in fact and statistically speaking, significantly reduce the risk of developing PCa. However, it should be noted that other 2 studies i.e., Dimitropoulou et al. [15] (United Kingdom), and Lozano-Lorca et al. (Spain), didn't mentioned any significance ($P>0.05$) of EF from SI to alter the risk (neither increase nor decrease). Conversely, EF from masturbation alone was observed to significantly increase the risk (only reported by Dimitropoulou et al. [15]), with estimated threshold of ≥ 2 tpw in 20s, ≥ 1 tpm in 30s,

and ≥ 1 tpw in 40s. Collective analysis on EF from both pooled SI and masturbation demonstrated a discrepancy between 3 studies, as Nair-Shalliker et al. [18], (Australia) concluded that ≥ 6 tpm increased the risk, Papa et al. [19] (Australia), documented that ≥ 14 tpw in the 30s decreased the risk, and yet Lozano-Lorca et al., didn't postulated neither outcomes.

The sub-group analysis of this outcomes partially revealed that the Europe-based investigation on PCa risk from SI-only EF doesn't underline significant outcomes, whereas the Iran- and Mexico-based stated the opposite. Furthermore, studies from Australia possessed variation in the outcomes as Nair-Shalliker et al. [18], and Papa et al. [19], concluded conflicting results regarding PCa risk from collective pooling of EF (including both SI and masturbation).

First sexual activity

The findings on FSA outcomes were more diversified, as we observed that 3 studies stated that higher (or older) FSA may increase the PCa risk, but the other 4 studies also stood with 'decreasing the risk' and 'doesn't change the risk' conclusions. Overall, the age of 16 to 17 years old is considered as a crucial threshold to influence the risk, considering some studies reported that FSA (either from SI or masturbation) older or younger than that may significantly increase or decrease the risk. For instance, Ahmadi et al. [11], and Angeles-Garay et al. [12], reported

Table 1. Characteristics of the Included Studies

Study	Location, obs. period, and study size (PCa/non-PCa)	Age (years old) PCa and non-PCa	Outcomes	Conclusion	NOS score
Ahmadi, [11]	Iran; May 2005 to Jan 2009; 194/317	71.0 ± 7.8 and 70.5 ± 10.2	Youth EF per month from sexual intercourse of ≤4, 5-12, >12 in PCa and non-PCa were 66.5 vs. 45.7, 23.4 vs. 31.9, and 10.1 and 22.4; respectively (P<0.001) FSA in PCa and non-PCa were 25.0 ± 5.6 and 23.9 ± 5.2; respectively (P=0.03)	Higher [A] decreases the risk Higher [B] increases the risk	6
Angeles-Garay, [12]	Mexico; Jan 2015 to Dec 2015 (261/522)	65.5 ± 6.4 and 66.0 ± 6.2	As compared to none EF from sexual intercourse at all per week: - Age <20s, EF of 1-2 and >2 per week have OR value of 0.92 and 0.51, respectively (P=0.001) As compared to 1 EF per week: - Age 20s, EF of 2 and ≥3 per week have OR value of 0.88 and 0.54, respectively (P=0.008) - Age 30s, EF of 2 and ≥3 per week have OR value of 1.41 and 1.50, respectively (P=0.07) FSA of 16-18 and >18 have OR value of 1.58 and 2.48, respectively (P<0.001) as compared to <16 FSA Lifetime SP of 5-9 and >9 have OR value of 0.65 and 0.57, respectively (P=0.002) as compared to 1-4 lifetime SP Lifetime female SP of 5-9 and >9 have OR value of 0.66 and 0.57, respectively (P=0.003) as compared to 1-4 lifetime SP	Higher [A] in <20s and 20s decreases the risk Higher [B] increases the risk Higher [C] in both sexes or female only decreases the risk [A] in 30s doesn't influence the risk	6
Chang, [13]	Taiwan; Feb 2018 to Dec 2020 (143/195)	72.6 ± 7.8 and 72.2 ± 7.7	Lifetime SP of ≤1, 2-3, and ≥4 was 32.2 vs. 48.1, 21.7 vs. 23.0, 46.2 vs. 28.9, respectively in PCa and non-PCa (P=0.007)	Higher [C] increases the risk	6
Cirakoglu, [14]	Turkey; Jan 2013 to Sep 2016 (146/171)	63.0 ± 8.1 and 66.2 ± 7.7	Youth EF from sexual intercourse per month in PCa and non-PCa were 10 (2-24) and 10 (3-30); respectively (P=0.236) FSA in PCa and non-PCa were 18 (13-52) and 20 (14-27), respectively (P=0.137) First masturbation age in PCa and non-PCa were 12 ± 16 and 15 ± 15 (P=0.018) Lifetime SP in PCa and non-PCa were 2 ± 6 and 1 ± 4, respectively (P=0.039)	Higher [B, first masturbation age] decreases the risk Higher [C] increases the risk [A] in youth doesn't influence the risk [B] doesn't influence the risk	6
Dimitropoulou, [15]	United Kingdom; NA (431/309)	43.0% and 33.6% in ≥ 56.5	As compared to EF from sexual intercourse ≤1 per week: - Age 20s, EF of 2-3 and 4-7 per week have OR value 1.03 and 1.03; respectively (P=0.852 and 0.900) - Age 30s, EF of 2-3 and 4-7 per week have OR value 1.15 and 1.05; respectively (P=0.410 and 0.831) - Age 40s, EF of 2-3 and 4-7 per week have OR value 0.95 and 1.02; respectively (P=0.787 and 0.939) As compared to EF <1 per month from masturbation: - Age 20s, EF of 1-4 per month and 2-7 per week have OR value 1.05 and 1.88; respectively (P=0.773 and 0.002) - Age 30s, EF of 1-3 per month and ≥1 per month have OR value 1.04 and 1.72; respectively (P=0.865 and 0.002) As compared to EF of 0 per month from masturbation: - Age 40s, EF of 1-3 per month and 1-7 per week have OR value 1.26 and 1.63; respectively (P=0.227 and 0.020) FSA of 20-24 have OR value of 0.71 as compared to <20 (P<0.03)	Higher [A] from masturbation increases the risk Higher [B] decreases the risk [A] from sexual intercourse doesn't influence the risk	8
Hennis, [16]	Barbados; Jul 2002 to Jan 2011 (963/941)	67.2 ± 9.0 and 67.0 ± 9.2	FSA in PCa and non-PCa were 17.3 ± 3.5 and 17.8 ± 4.2; respectively (P=0.01) FSA percentages of <16, 16-18, 19-21, and >21 in PCa and non-PCa were 29.3 vs. 24.9, 41.0 vs. 41.3, 20.8 vs. 21.8, and 8.8 vs. 21.0; respectively (P=0.01) Lifetime SP from PCa and non-PCa were 12.0 ± 29.0 and 10.5 ± 19.5; respectively (P=0.28) Lifetime SP percentages of 0-3, 4-9, 10-20, and >20 in PCa and non-PCa were 25.0 vs. 27.0, 40.7 vs. 41.8, 23.5 vs. 23.0, and 10.8 and 8.2; respectively (P=0.12)	Higher [B] decrease the risk [C] doesn't influence the risk	7

Abbreviations: EF, Ejaculation frequency (can be interpreted into intercourse-related, masturbation-restricted, or unspecified EF; and denoted in [A]); FSA; First sexual activity (age; in years, denoted in [B]); mainly representing intercourse, but might also demonstrated first masturbation age in some studies); OR, Odd ratio; PCa, Prostate cancer; SP, Sexual partner (denoted in [C])

Table 1. Continued

Study	Location, obs. period, and study size (PCa/ non-PCa)	Age (years old) PCa and non-PCa	Outcomes	Conclusion	NOS score
Lozano-Lorca, [17]	Spain; May 2017 to Sep 2020 (456/427)	66.2 (62.2-72.1) and 68.4 (62.7-73.9)	The observed EF from both intercourse and masturbation per months percentage during lifetime - Age 20s, EF of 0-3, 4, and >4 was 91.3 vs. 95.5, 5.7 vs. 3.5, and 2.0 vs.0.9 in PCa and non-PCa, respectively (P=0.045) - Age 30s, EF of 0-3, 4, and >4 was 93.8 vs. 96.7, 5.3 vs. 2.6, and 0.9 vs.0.7 in PCa and non-PCa, respectively (P=0.117) - Age 40s, EF of 0-3, 4, and >4 was 78.2 vs. 75.3, 19.6 vs. 21.9, and 2.2 vs.2.8 in PCa and non-PCa, respectively (P=0.569)	[A] doesn't influence the risk	8
Nair-Shalliker, [18]	Australia; Jan 2006 to Dec 2014 (1,181/875)	46.1% in 60-69 and 30,6% in 60-69	Youth EF from both intercourse and masturbation per month of 4-5 and ≥6 per month have OR value of 1.33 and 1.59, respectively (P>0.05 and <0.05) as compared to 0-3 EF FSA of <17, 17-19, and 20-22 have OR value of 1.68, 1.52, and 1.20, respectively (P<0.05, <0.05, and >0.05) as compared to >22 FSA Lifetime SP of 3-7 and >7 have OR value of 1.15 and 2.00, respectively (P>0.05 and <0.05) as compared to <3 lifetime SP	Higher [A] of ≥6 per month increases the risk Higher [B] decreases the risk Higher [C] of >7 increases the risk [A] of 4-5 doesn't influence the risk to 0-3 [B] of 20-22 doesn't influence the risk to >22 [C] of 3-7 doesn't influence the risk to <3	7
Papa, [19]	Australia; Jan 2010 to Jun 2014 (1,236/905)	66.7 (62.1-70.3) and 62.8 (58.0-67.4)	No significant difference in EF from both intercourse and masturbation per week in age 20s to 40s (P=0.50, 0.06, and 0.90; respectively) As compared to EF <7 per week: - Age 20s, EF of 7-13 and ≥14 per week have OR value of 1.04 and 1.09, respectively (both P>0.05) - Age 30s, EF of 7-13 and ≥14 per week have OR value of 0.96 and 0.55, respectively (P=0.80 and 0.013) - Age 40s, EF of 7-13 and ≥14 per week have OR value of 0.80 and 0.97, respectively (both P>0.05)	Higher [A] of ≥14 per week in the 30s decreases the risk [A] in 20s and 40s don't influence the risk [A] of 7-13 doesn't influence the risk in 30s	7
Spence, [20]	Canada; Sep 2005 to Aug 2009 (1,590/1,618)	50.6% in 60-69 and 48.6% in 60-69	FSA of 17-18, 19-21, and ≥22 have OR value of 1.05, 1.08, and 1.15 as compared to ≤16 FSA; respectively. But all P>0.05. Lifetime SP (both gender) of 2-3, 4-7, 8-20, and ≥21 have OR value of 0.92, 1.02, 0.91, and 0.78; respectively as compared to 1 SP (P>0.05) Lifetime female SP of 2-3, 4-7, 8-20, and ≥21 have OR value of 0.91, 0.97, 0.89, and 0.72; respectively as compared to 1 SP. But only ≥21 SP have significant effects (P<0.05) Populations with no sexual intercourse has an OR value of 1.94 as compared to 1 SP (P>0.05) Populations with lifetime male only SP has an OR value of 2.53 as compared to 1 SP (P>0.05)	[B] doesn't influence the risk Neither female or both sexes [C] of 2-3, 4-7, and 8-20 influence the risk No [C] or male only don't influence the risk Higher female [C] of ≥21 decreases the risk	8

Abbreviations: EF, Ejaculation frequency (can be interpreted into intercourse-related, masturbation-restricted, or unspecified EF; and denoted in [A]); FSA; First sexual activity (age; in years, denoted in [B]; mainly representing intercourse, but might also demonstrated first masturbaion age in some studies); OR, Odd ratio; PCa, Prostate cancer; SP, Sexual partner (denoted in [C])

higher FSA age among PCa patients (or higher PCa percentage among older FSA group), with PCa patients experienced first sexual activity in relatively older age (25.0 ± 5.6 years old vs. 23.9 ± 5.2 ; P=0.03 in Ahmadi et al.'s investigation., and higher proportion of PCa incidence among individuals with FSA >16 years old based on the report by Angeles-Garay et al. [12], in 2019 (the OR were 1.58 and 2.48 in 16-18 years old and >18 years old; respectively, compared to FSA <16 years old).

In other hand, Hennis et al. [16], (Barbados) and Nair-Shalliker et al. [18], documented that PCa populations have younger or earlier FSA age (e.g., 17.3 vs. 17.8 years old in Hennis et al. [16] and higher proportion of PSA among individuals that initiated sexual activity at <17 and 17-19 years old compared to >22 years old FSA

in Nair-Shalliker et al.'s. [18] investigation). Followingly, Dimitropoulou et al., also recorded that population with FSA in their 20-24 years old possessed significantly lower OR compared FSA <20 years old individual (OR=0.71; P=0.03 in 95% CI). Conversely, Cirakoglu et al. [14], (Turkey) and Spence et al. (Canada), noted that FSA might not be that important in altering the risk overall, as they observed that no significant difference among various FSA groups (P>0.05). Yet, Cirakoglu et al. [14], also stated an interesting finding of lower FSA age through masturbation or self-induced ejaculation might in fact, increase the risk significantly (mean FSA from masturbation; 12 ± 16 years and 15 ± 15 years old in PCa and its comparator; respectively). The geographical sub-group analysis doesn't demonstrate any remarkable outcomes from this

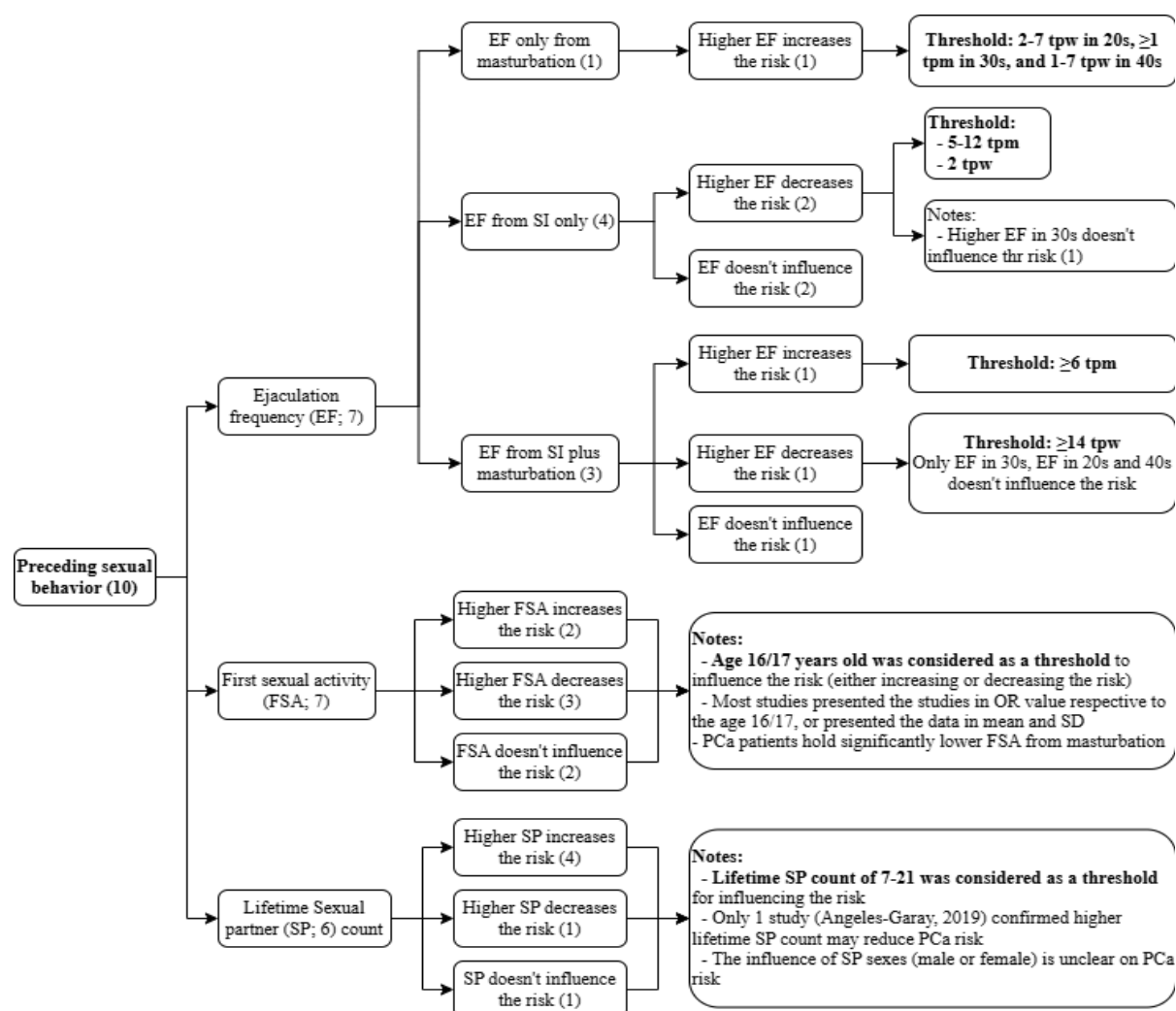


Figure 2. Schematic Representation of Our Qualitative- and Systematic-Review to Elaborate the Influence of Sexual Behavior in Younger Years in Causing Prostate Cancer

study, as almost all investigations with similar results were originated from different regions.

Sexual Partner

Our qualitative assessment on the studies basically underlined that most of the findings confirmed there were remarkable association between higher SP count toward PCa risk; with at least 4 out of 6 studies supported the premise. The lifetime SP count of 7 to 21 was considered as a 'threshold' interval to develop significant increase in PCa risk, though it is estimated that there was a possibility of 'dose-dependent' relationship, with higher lifetime SP count may correspond to increase in PCa risk due to various reasons. Interestingly, Angeles-Garay et al. [12], reported a contrary result, with higher lifetime SP count may decrease the risk of PCa significantly, as represented by lower OR value among individuals with SP count of 5-9 (0.65) and >9 (0.57) compared to individuals with <5 SP count; with $P=0.0002$ in 95% CI. Moreover, the true influence of SP gender remains unclear in this study, with Angeles-Garay et al. [12], documented that higher lifetime female SP count may reduce the PCa risk, supported by the findings in Spence et al. [20], which

estimated that individuals with >21 sexual partner has significantly lower OR value (0.72; $P<0.05$ in 95% CI) compared to individuals with only a single SP. Similar to the FSA outcome, geographical sub-group analysis of the SP count also demonstrated variation in the regions, as studies confirming higher SP increases the risk were originated from Australia, Canada, Taiwan, and Turkey; four countries from different continent with different socio-cultural background as well. In other hand, these variations may even suggest that the influence of higher SP count to PCa risk is more than just a socio-cultural phenomenon, but also involving the biological nature of multi-partner intercourse in modern society.

Discussion

Controversial and undoubtedly challenging to be proven, yet, the necessity to provide answers on delineating the influence of sexual behaviors in younger years to individuals' well-being in later life should remain important; especially in current modern society with access to sexual health knowledge is more liberated than ever. As mentioned earlier, our review was initiated with

a simple but common inquiry among males: “How much is too much?”, for the context is a rough estimation of ideal ejaculation rate per week (or month), regardless its preceding activities i.e., self-induced (masturbation) or engaging a SI session. For ages, or at least in the last decades, the main hypothesized concern of frequent masturbation (in an extremely frequent manner) is an increase in possibility to develop an agonizing consequence toward its sexual organ e.g., prostate cancer (PCa). Theoretically, responding such question could be done in two different approaches: conducting an investigation with decades of follow-up to acquire nearly-correct and specific sexual behavior characteristics until the cancerous growth prevails; or relying on the currently PCa-diagnosed individuals’ “confession” of its sexual activities in younger years, in which the latter are being attempted to be reviewed in narratives.

Acknowledging the most apparent limitation in our review i.e., recall bias is the first step to understand the findings, as this study is heavily relied on subjective report by the patients on their sexual experience in younger ages. Nevertheless, the outcomes of this qualitative analysis can be break down into three main postulations: (1) High EF (from SI only) may reduce PCa risk with an estimated threshold of 5-12 times per month (tpm) or 2 times per week (tpw), but including masturbation into the populations sexual experience has a considerable potential to be resulted in unfavorable outcomes (e.g., the estimated cut-off of masturbation only was 2-7 tpw in their 20s) [11–17]; (2) The influence of FSA were the most inconsistent findings in our study as no apparent conclusion can be drawn from difference in FSA, though a study [13] confirmed that PCa patients have earlier FSA from masturbation [11–14, 16, 18, 19]; and (3) Higher SP count almost certainly directed adverse influences to the PCa risk which mostly hypothesized to be originated from sexually-transmitted infections (STIs) e.g., human papillomavirus (HPV), gonorrhea, syphilis etc. and its attributed immunoreactive effect on the prostate. These findings indirectly underlined that the occurrence of PCa isn’t limited to the interplay between non-modifiable risk factors and classical diet-smoking-sedentary lifestyle triads, but should also consider “unhealthy” preceding sexual behaviors.

As interesting as it may implicate, the idea of sexual behaviors to partake into PCa pathogenesis is hypothesized by increased androgenic activity among sexually-frequent individuals, which theoretically cause the prostate to be more biologically receptive and proactive of endogenous testosterone’s influences. Furthermore, earlier sexual exposure to an individual may indicate a relatively higher sexual experience rate in general population, either by masturbation or even by engaging in active SI with its respective partner(s) [3, 20, 21]. This idea corresponds with increased prostatic activity in possibly younger ages, along with the additional socioeconomic factors that contribute significantly to the phenomenon. For instance, teenage marriages or early SI among teens are correlated with lower socioeconomic status (mostly driven by patriarchal norms as soon as the teen is able to become economically-independent), which eventually in track

with the other PCa’s risk factors e.g., sub-standard diet, smoking, and even sedentary lifestyles [22, 23]. Its “dose-dependent” correlation has been described in a meta-analysis by Jian et al., in 2018, as the study documented higher SP count and younger FSA were associated with increased PCa risk; though the true influence of EF remains questionable at the end of study [8].

To add-up the discussion, another proposed theory also includes reduced ejaculation rate (which can also represent overall sexual activity rate) might become an influential risk factor of PCa. The latter hypothesis lies on an accumulation of carcinogenic-inducing agents’ deposition in prostatic acini due to “stagnation” of the organ’s byproduct; hence termed the ‘prostate stagnation theory’. For that mechanistic-biologic reason, frequent ejaculation may induce a “flushing” phenomenon of potentially carcinogenic substances that accumulate in the prostate gland, potentially preventing buildup of cancer-supporting microenvironment [15, 24, 25]. Variation in one of the most stand-out outcomes is unquestionably an intriguing prospect to be elaborated even further, as it remains unclear whether an individual may benefit from performing substantial counts of ejaculation to reduce PCa risk in the future, or even a nearly-sexual abstinence state is the best condition to avoid the malignancy? Hypothetically, the cells’ turnover rates will be relatively minimal compared to sexually active prostates, yet, how should we define an ideal sexual behavior to deter neoplasm transformation of the prostate? Which in turn will also reduce the cancerous growth risk of the organ as the results of determining a reasonable guide for sexual activities? Interestingly, Kobori et al. [28], documented that the serum testosterone level underwent significant rise approximately 10 minutes after masturbation, but it will return to the baseline as soon as the period is over (along with cortisol and prolactin levels). The latter study along with Isenmann et al. [27], stated that masturbation may affect free testosterone concentrations, though the hormonal ratios remain unchanged [26, 27]. Acquiring recommendations on optimal EF rate may eventually require a long-term observation, though we had attempted to grasp the available evidences on determining optimal EF rate weekly (or monthly).

Although our study indirectly confirmed that higher EF should be considered as a protective variable of PCa occurrence, it should be underlined that its favorable outcome was exclusive from SI-related EF only. Whilst interpretation on the masturbation’s impact of advises limiting the sexual experience to some extent (e.g., 2-7 tpw based on the findings from reviewed studies), it should never be rejected that self-induced ejaculation can be considered healthy, only if the frequency remains on the “acceptable” rate and not approaching “extreme” addiction. Our study might encourage routine ejaculation for at least 2-7 tpw or 5-12 tpm based on the current evidence, for it is advised to acquire such experience in partnered sexual activity to achieve possibly favorable results. Furthermore, we also highlight the important of responsible sexual experience initiation, for younger FSA ($\pm 16/17$ years old) might increase the PCa risk significantly and remarkably older FSA (e.g., in 30s,

etc.) is also correlated with PCa occurrence, denoting predispositions to develop PCa among individual with extreme FSA [28, 29]. Interestingly, association between older FSA and PCa risk might be correlated with poorer socioeconomic factors (and unwell biologic factors i.e., chronic illnesses), as the individuals may experience higher count a of masturbations, plus lower social- and economic-status that “force” the males to engage in SI much later [30]. Moreover, extreme FSA is also correlated with unhealthy ideation of sex and expectations from the activity, along with the role of possible mental illness e.g., depression that are also associated with PCa risk (or the other malignant transformation as well). To exemplify the situation, co-existing mental health issues is correlated with sub-standard lifestyles and socioeconomic factors (along with awareness to the individuals’ health condition) [31, 32].

Further analysis on the influence of SP count toward PCa risk demonstrated a theoretically sound result, as higher lifetime SP count of approximately 7-21 different individuals (regardless the genders) has detrimental effects on PCa occurrence. The most perceivable reasoning for this phenomenon can be defined into two major causes e.g., (1) the role of STIs in PCa pathogenesis and (2) increased sexual activity rate among individuals with higher lifetime SP count. Initially, the relationship between STIs and PCa is a vague yet intriguing topic. Chronic inflammation on the organs, with no exception on the prostate, has been heavily linked to induce biological changes in the organ’s microenvironment, plus, the microbes also wield potentials to contribute in prostate carcinogenesis through multiple mechanisms e.g., damaging the DNA in cells and/or impairing immunological responses to neoplasm transformation. However, the EPICAP (Epidemiological Study of Prostate Cancer) study suggested the contrary results, as Sawaya et al. [33], mentioned that the role of bacterial or viral infections of the genitourinary tract in PCa should be investigated further, as they underlined the necessity to add the focus on evaluating chronic inflammation states instead. The latter findings were also supported by Dennis et al. [34], in their investigation among males drafted in US military setting, as they concluded a “little-to-none” association between presentation of previously detected antibodies for HSV-2, HPV types, and *C. trachomatis* to the current PCa diagnosis. Another cancer screening trial by Huang et al., also agreed upon inconsistent association of specific STIs to PCa incidence among pathogens (e.g., findings of antibodies of *C. trachomatis* are positively correlated with PCa diagnosis), signifying the need to perform investigation that wasn’t limited to STIs, but also the sexual functioning itself (especially EF or other parameters of sexual behavior) [34].

Extending the evaluation to the individuals’ sexual orientation can also be classified as part of behavioral aspect of sex, as emerging theories are equally captivating to be elaborated even further. For instance, homosexual males who engage in anal intercourse (or history of male partners) theoretically have higher risk of PCa through multiple mechanisms e.g., chronic micro-trauma of the prostates or unsafe sexual activities that eventually leads

to STIs (or other inflammatory condition though the idea of “sexually-transmitted”-PCa remains inconsistent to date) [35, 36]. An included study in this review by Spence et al., observed that sexual orientation has no remarkable impact on PCa occurrence [20]. Rosser et al. [37], in their narratives also stated that evaluation among homosexuals with PCa appears to be screened significantly less compared to the heterosexuals, though necessity for providing such study to create an ideal sexual experience among males is unequivocally important. With advance on the current non-invasive PCa testing through the notorious “liquid-biopsy” or urine-based approach, repetitive screening on ‘in-risk’ groups plus the ‘sexually-perilous’ individuals should be possible in the future. Theoretically, this urine-based testing may detect pathological changes thorough an individual’s sexual journey, as we able to quantify, or at least identify “fluctuation” of the urinary contents [38–40]. Though the current evidence is limited to draw a line between urinary content, sexual behavior, and its respective neoplasm-transformation risk, the opportunity to conduct prospective studies on the issues remains open through this view point.

Despite our attempt to provide a comprehensive qualitative mapping of sexual behaviors and their influence on prostate cancer risk, several limitations should be acknowledged. First of all, the retrospective nature of the included studies introduces recall bias, as participants may inaccurately report their past sexual behaviors, leading to potential misclassification. Our review also omitted quantitative meta-analysis considering its main objective to provide a ‘qualitative-mapping’ with minimal novel mathematical output; though we acknowledged the statistical findings from the evaluated studies to increase the analytical depth. Additionally, cultural differences in sexual norms and reporting practices across study populations may affect generalizability. The biological mechanisms underlying the associations remain speculative, requiring further investigation through prospective cohort studies with long-term follow-up and objective hormonal assessments. Future research should aim to establish standardized measures for defining “healthy” sexual behavior, considering not only ejaculation frequency but also contextual factors such as partner dynamics, age of initiation, and the role of sexually transmitted infections. Clarifying these aspects will be essential in formulating evidence-based recommendations on sexual health that balance potential protective and risk factors in prostate cancer prevention.

In conclusions, our qualitative review highlights the complex relationship between sexual behaviors in younger years and prostate cancer risk, emphasizing ejaculation frequency, age at first sexual activity, and sexual partner count as key influencing factors. While higher ejaculation frequency from SI may confer a protective effect, excessive masturbation appears to increase risk, suggesting a differential impact based on sexual activity type. The role of first sexual activity remains inconclusive, whereas a higher number of lifetime sexual partners is generally associated with increased prostate cancer risk, potentially due to sexually

transmitted infections and chronic inflammation. Despite limitations related to recall bias and study heterogeneity, our findings underline the importance of further prospective research to refine guidelines on healthy sexual behaviors. Future investigations should aim to establish clear recommendations balancing sexual health and prostate cancer prevention, integrating biological, behavioral, and socioeconomic considerations.

Author Contribution Statement

Conceptualization: NNF, SMW; Methodology: NNF, SMW; Software: NNF, AJV; Validation: SMW, GPS, DDK, FFP; Formal Analysis: NNF, SMW, AJV; Investigation: NNF, SMW, GPS; Resources: NNF, AJV; Data Curation: NNF, SMW, FFK, FFP; Writing – Original Draft: NNF, SMW, AJV; Writing – Review & Editing: NNF, SMW, DDK, FFP; Visualization: NNF, AJV, DDK; Supervision: SMW, FFP; Project Administration: NNF, SMW; Funding Acquisition: SMW, AJV.

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