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PHARMACOTHERAPY BASED ON MEDICAL GENETICS FOR SMOKING CESSATION

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Abstract: Indonesia is the fourth highest consumer of cigarettes in the world with an estimated high cost in healthcare expenditure on tobacco-related diseases. Nonetheless, regulations on tobacco products are lax and healthcare provider involvement in aiding smoking cessation is minimal. Generally, a variety of smoking cessation aids exists and medical genetics have come into play to enhance their efficacy. A questionnaire survey was piloted to query participants on their smoking habits, past cessation attempts, opinions on factors related to smoking cessation, and reactions to information that medical genetics could provide within the context of smoking cessation. The findings showed that most participants have attempted cessation without aid. Pharmacotherapy was not used by any respondents while behavioral interventions were scarcely used. Nevertheless, 83% of participants indicated that medical genetics information would be useful in future cessation attempts and that they would consult physicians for advice.

Keywords: smoking; cessation; nicotine; addiction; pharmacotherapy.

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1. INTRODUCTION

The tobacco industry has a significant and active role in Indonesia due to the country's lax regulations on tobacco product advertisement and its low tobacco taxation [1,2]. Aside from non-stringent government regulations and the aggressive marketing by tobacco companies, the act of smoking is deeply ingrained in the Indonesian people's daily lives and social culture. Indonesia is the fourth highest cigarette consumer in the world, after China, Russia, and the US [3]. The lack of excise tax regulations on tobacco products leads to low cigarette prices in Indonesia. This creates a ripple effect of decreased quality of life, especially amongst low income communities. A regular pack of twenty cigarettes cost under USD \$2 in Indonesia, with some brands closer to \$1 per pack [3]. It is estimated that an average low-income household spends 15 times more on tobacco than on healthcare and 9 times more on tobacco than on education. Tobacco purchase (12% of total monthly spending) takes precedence over utility bills (water, electricity, phone bills), housing rent, and protein food sources; cigarette spending trails behind only the purchase of rice (22% of total monthly spending) [2]. According to a joint WHO and World Bank study in 2011, 5% of GDP per capita is spent on buying an average of 100 packs of cigarettes.

As of 2011, approximately 60 million people in Indonesia smoke cigarettes on a daily basis with an average cigarette consumption of 12-13 sticks per day [1,2]. Smoking initiation typically begins around the ages of 17-18 with almost 13% of smokers beginning before the age of 15 [2]. Gender-wise, more male Indonesians smoke (57%) than females (4%). However, all population sub-groups, particularly children, are affected by the serious and negative impact of second-hand smoking (SHS) exposure. Close to 134 million non-smokers in Indonesia are exposed to SHS regularly, which is not surprising given that over 70% of Indonesians live in a household with at least one smoker [2,4].

Additionally, the lack of smoking bans in public places exposes many individuals to SHS at their place of work and most social and public places. Tobacco-attributed death is estimated to be over 200,000 annually in Indonesia. One in five male deaths and one in ten female deaths are traced back to regular smoking consumption and/or exposure [3]. The main causes of tobacco mortality in Indonesia are cardiovascular diseases, malignant cancers (particularly lung), and

chronic, obstructive respiratory illnesses [4]. Approximately, 11 trillion Indonesian rupiah (1.2 billion USD) per year is spent on medical care related to tobacco-attributed diseases [4]. Non-smoking women exposed to SHS at home have an estimated 25% increased risk for lung cancer and an estimated 23% to 25% increased risk for cardiovascular diseases [4].

With nicotine addiction being tied closely to brain chemistry, pharmacotherapy is the most effective method to alleviate withdrawal symptoms, especially for moderate smokers [5]. Several pharmacotherapies for smoking cessation, such as nicotine replacement therapies, varenicline, and bupropion, have been shown to be effective treatments, especially when used in combination [6,7]. Their availabilities vary considerably throughout the world [8]. Behavioral therapies are common aids for smoking cessation as well, such as medical counseling (in-person or remote counseling) and support group meetings [9]. Using behavioral therapy in combination with a form of pharmacotherapy protocol has a small but significant impact, increasing success rate by 10-25% compared to pharmacotherapy approaches alone [10].

Given the complexity of nicotine addiction [11], the wide array of treatment approaches [7], and the cost of development of new therapies [12], improvements of currently available treatments is a priority [5,13]. With medical genetics being applied to smoking cessation, selecting the most effective treatment protocol for individual smokers is becoming possible [14]. For example, assigning treatment by an individual's nicotine metabolism, has been shown to improve effectiveness of varenicline and nicotine patch [15]. In addition, genetic variants in the *CHRNA5* nicotinic receptor have been shown to influence the efficacy of various nicotine replacement therapies [16]. The refinements of treatment protocols based on medical genetics information may improve the likelihood of cessation and minimize side effects [17]. With rapid advancements in technology and decreasing cost in DNA sample collection and processing, many facets of smoking cessation therapy can be improved through genetic-based screening [18].

In this article, we present results from a survey designed to better understand the relationship between high smoking rates in Indonesia and the general availability of a variety of cessation treatments and screening methods. Motivated by the health impact of smoking, the questions

were designed to help characterize smokers in Indonesia, particularly in their experiences towards smoking cessation attempts and methods, as well as in their opinions towards factors influencing smoking cessation and medical genetics.

2. METHODS

This survey was funded by Bina Nusantara University to survey opinions on smoking cessation ability, as well as beliefs on factors that influence cessation success. The 31-question survey was developed to capture information on smokers in three areas: demographics, smoking behavior, and smoking cessation. Current smokers were recruited in 2015 from the greater Jakarta metropolitan area due to its proximity to the Bina Nusantara University campus. Occupations were categorized based on Indonesia's official government identification card; the categories are: civil servant, entrepreneur, educator, and, student. None of the occupations were targeted specifically. There were 111 participant smokers. Preliminary question asking smokers on their willingness to participate was administered. Upon agreement, a hardcopy of the questionnaire was used as a data collection instrument. The questionnaire was self-administered and completed primarily at workplace and campuses (for students) with a few completed at public places such as restaurants and food courts. To reduce incompleteness in survey responses, trained interviewers verified missing responses with participants were due to refusal to give a response rather than an oversight. Gathered data were entered from hard-copy questionnaires into a database that was maintained with mySQL [19]. The descriptive statistics were generated with R [20].

3. RESULTS AND DISCUSSION

There were 111 participant smokers completed the survey. The demographics of the participant are summarized in Table 1. The age range of participants was between 18 and 60 years old (mean of 32.4 years old). Over 90% of the participants were males and over half (51%) were married. Additionally, most were office workers and students (70%), head of households (47%), and have at least a high school education (95%). Most of participants (37%) had household size of four.

Table 1. Participant demographics

Average age (SD) in years	32.4 (11.7)
Sex	Count (%)
Male	92 (83)
Marital status	
Married	53 (51)
Occupation	
Entrepreneur	5 (5)
Office worker	42 (38)
Civil servant	8 (7)
Student	36 (32)
Educator	18 (16)
Other	2 (2)
Role in household	
Head of household	52 (47)
Wife	5 (5)
Child/dependent	54 (49)
Highest level of education	
Elementary school or less	3 (3)
Middle school	3 (3)
High school	49 (44)
Bachelor's and beyond	56 (51)
Household Size	
Two	13 (12)
Three	19 (17)
Four	40 (37)
Five	26 (24)
Six	6 (6)
Over six	4 (4)

Table 2 summarizes the smoking habits of the participants. 47% smoked between 10 and 19 cigarettes per day while 20% were heavy smokers (over 20 cigarettes per day.) We found that 75% of the surveyed participants have attempted to quit smoking at least once. However, only 16% of those who had attempted were successful in maintaining their cessation for over six months (see Table 3); even then, these participants had relapsed and had continued smoking since all participants in the survey were current smokers. 26% of the survey participants reported to have had an illness due to smoking and 19% reported to have sought medical care related to smoking. Approximately two third of participants (64%) spent between Rp 100,000 (USD 7.50) to Rp 500,000 (USD 37.50) on monthly cigarettes expense.

Table 2. Smoking-related characteristics

Smoking initiated (years ago)	Counts (%)
< 5	24 (22)
5 - 10	28 (26)
11 - 20	31 (28)
21 - 30	14 (13)
> 30	12 (11)
Cigarettes per day	
< 10	36 (33)
10 - 19	51 (47)
20 - 29	18 (17)
≥ 30	3 (3)
Monthly cigarette expense	
< Rp 100,000	23 (22)
Rp 100,000 - 300,000	38 (36)
Rp 300,000 - 500,000	30 (28)
> Rp 500,000	16 (15)
Illness due to smoking	
Has occurred	29 (26)
Have not occurred	82 (74)

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Medical care sought related to smoking	
Yes	21 (19)
No	90 (81)
Cessation attempted	
Yes	82 (75)
No	28 (25)

Table 3 further divides the participants based on whether they had attempted smoking cessation or not. For those who had attempted cessation, social environment (36%) and withdrawal symptoms (41%) were the most frequently selected responses for why they believed that their attempts failed. Most quit attempts were unaided (74%) and no participant used pharmacotherapy to attempt quitting. While only 3 (4%) smokers attended a smoking cessation clinic, 11 (14%) smokers received consultation from a doctor, indicating the need of increasing the involvement of primary care providers in smoking cessation. Nearly four-fifths of those who never attempted cessation stated that they wished to quit smoking in the future. 39% felt they could quit with no aid, while 44% admitted that their addiction is the primary reason they have not attempted to quit. Few smokers were aware of screening using medical genetics for cessation in both groups.

Table 3. Questions on smoking cessation attempts*

Have Attempted to Quit (N = 82)*		Have Not Attempted to Quit (N = 28)*	
Reason for quit attempt	Count (%)	Reason for no quit attempt	Count (%)
Social or family urging to stop	18 (22)	Feel in control/no need	15 (56)
Health reasons/want to be healthier	52 (63)	Addiction/need to smoke	12 (44)
Financial reasons	12 (15)	Quit in the future	
First quit attempt (years ago)		Yes	22 (79)
< 5	60 (74)	No	6 (21)
6-10	8 (10)	Method if quitting in the future	
> 10	13 (16)	Rehabilitation	0 (0)
Quitting method		Smoking cessation clinic	4 (14)
Rehabilitation	4 (5)	Pharmacotherapy	2 (7)

Smoking cessation clinic	3 (4)	Doctor consultation	7 (25)
Pharmacotherapy	0 (0)	Hypnotherapy	4 (14)
Doctor consultation	11 (14)	No aid	11 (39)
Hypnotherapy	3 (4)	Involve medical treatment	
No aid	59 (74)	Yes	10 (36)
Attempt outcome		No	18 (64)
Successful	13 (16)	Aware of medical genetics for cessation	
Not successful	69 (84)	Yes	5 (18)
Reason for non-success		No	23 (82)
Social pressure	22 (36)		
Cannot overcome withdrawal symptom	25 (41)		
Relapse for other reason	14 (23)		
Aware of medical genetics for cessation			
Yes	9 (11)		
No	73 (89)		

*Participants who refused to respond on whether cessation has been attempted or not were excluded

Table 4 lists responses on perception on how certain factors affect cessation ability as well as responses to positive and negative reactions to outcomes related to medical genetics and smoking cessation ability. Social environment, exercise, stress level, and satisfaction gained from smoking were the most frequently selected factors in terms of importance on cessation difficulty. Most participants disagreed that they would feel hopeless if they were to find out via medical genetics that cessation would be difficult. Many also responded that they would want to find out more about their children's and family risk of addiction and ability to quit smoking. Overall, 83% of the smokers felt that genetic screening would be useful if it could indicate cessation difficulty and would lead to their consulting their doctors for advice. The majority of responders were interested in knowing the conditions that could be assessed through medical genetics in relation to smoking cessation (64%) and smoking-related risks (57%). However, reports on higher likelihood of suffering from cardiac arrest, a known smoking risk factor, would have no effect in motivating lifestyle changes in over three-quarters of the respondents.

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Table 4. Opinions and attitudes towards factors that potentially influence smoking addiction and cessation ability*

Factors on smoking cessation ability	Not important (%)	Important (%)	
Diet	64 (59)	45 (41)	
Exercise	33 (30)	76 (70)	
Social	16 (15)	92 (85)	
Culture	45 (42)	63 (58)	
Alcohol	60 (55)	49 (45)	
Drugs	62 (57)	47 (43)	
Insurance	65 (60)	43 (40)	
Luck	78 (73)	29 (27)	
Stress	21 (19)	88 (81)	
Ethnicity	91 (84)	18 (16)	
Satisfaction from smoking	19 (18)	89 (82)	
Response to medical genetics information on cessation difficulty	Agree (%)	Disagree (%)	
No hope of ever quitting	14 (13)	92 (87)	
Determine if offspring has same risk	79 (74)	28 (26)	
Advice other family not to smoke	99 (92)	9 (8)	
Feel that a genetics test was useful	90 (83)	18 (17)	
Consult a doctor for quitting method	90 (83)	18 (17)	
Conditions of interest for genetic report	Yes (%)	No (%)	
Higher risk for lung cancer/diabetes/cardiac arrest	60 (57)	46 (43)	
The best method for smoking cessation	70 (64)	39 (36)	
Have lower risk for lung cancer despite smoking	64 (59)	44 (41)	
Effect of knowing higher cardiac arrest likelihood	More likely (%)	Less likely (%)	Same (%)
Quit smoking	12 (11)	11 (10)	83 (78)
Reduce smoking level	10 (10)	12 (12)	82 (79)
Increase exercise frequency	7 (7)	11 (10)	88 (83)

*Total responses for each question does not necessarily yield N = 111 since some participants refused to provide a response

This survey has characterized current smokers within an urban city in Indonesia, namely Jakarta. The questions of the survey encompassed participants' cessation attempts and opinions on factors influencing cessation abilities. As is often the caveat with surveys, there were some notable limitations. The sample was generally small due to the labor-intensive process to recruit and minimize missing information from each participant. The survey was also conducted in only in Jakarta due to the location of Bina Nusantara University and convenience. Therefore, generalizability of findings to other areas of Indonesia is limited. In general, participants tended to give more general responses until asked to be more specific. For instance, when responding to how many years ago smoking was initiated, many participants responded with a range rather than a specific number of years.

Despite the seemingly common knowledge of risks associated with smoking, it is still prevalent worldwide and in Indonesia. Smokers tend to underestimate their susceptibility to diseases caused by smoking and are unaware of many facets of how smoking is dangerous [21–23]. Among the major risk factors of smoking is sudden cardiac arrest [24]. However, we found that few respondents reported that this would motivate them to quit or change their smoking habit if they were informed by medical genetics to be more susceptible towards a cardiac arrest event. Instead between 78-80% responded that it would have no effect on their behavior (see Table 4).

Surveying a target population before introducing medical screening or treatments is important to avoid misinformation and skepticism [25,26]. Therefore, evaluating the opinions and attitudes of Indonesian smokers towards smoking cessation and medical genetics is essential for program development. We showed that assumptions on common knowledge about the dangers of smoking or ways to quit smoking should not be made. In this survey, it was found that a majority (little over two-thirds) of the participants plan on quitting in the future, mainly without any form of assistance. For those who have attempted cessation, none stated that they used pharmacotherapies. With these responses, it was sensible that very few were also aware of the utility of medical genetics for smoking cessation.

The use of pharmacotherapy is an effective way to assist smokers during the onset of withdrawal symptoms, especially given that cravings were reported as the main reason for a non-successful cessation attempt and as the reason for never attempting to quit. Therefore, pharmacotherapy can be beneficial for Indonesian smokers, helping them overcome nicotine withdrawal symptoms. In addition to genetics, cessation ability is heavily influenced by environment, lifestyle, and psychological factors [27]. Based on the survey, Indonesians are more aware of psychosocial and lifestyle factors but not the biological factors that influence smoking cessation. They believed that social environment, exercise, and stress were the most important factors influencing cessation success. As a result, medical consultation and support groups could benefit Indonesian smokers attempting cessation as well.

Several questions were included in the questionnaire to evaluate the reaction towards good and bad news from a genetic test. Based on the survey, Indonesians would reap more benefit than harm from the results of a genetic test stating that they would have difficulties with smoking cessation. Additionally, the majority of respondents stated that they would not feel hopeless upon finding out that they had higher risk for smoking-related diseases. Gauging how smokers believe they could benefit from medical genetics is important [26]. The survey found that the information that interests Indonesian smokers the most is to determine the best cessation method for them. There was also interest in determining their level of risks for smoking-related diseases.

Beyond benefits for themselves, most of the participants stated that they would like to know if their children had the same predispositions and would encourage their families and friends to quit smoking. Previous studies have shown that smokers having more concern over whom they affect than themselves; particularly when their children are involved [28]. Children as a motivation for cessation could be particularly useful since many Indonesian smokers are heads of households living in homes with 3-5 members.

The survey discovered that genetic screening would encourage smokers to seek medical help. Initial implementation should be done cautiously to avoid the “magic bullet” perception and any other misperception on the capabilities of any single method of treatment [29,30]. The greatest

barrier would be raising awareness and educating the population on treatments available for them; this in turn poses a significant barrier to adding medical genetics to smoking cessation therapy. None of the surveyed participants used pharmacotherapy in their cessation attempts. This was expected given that nicotine replacement therapies, such as patches and gums, are not available in Indonesia but are available in neighboring countries, such as Singapore [31] while varenicline is available in Indonesia but at a steep price [32].

There is a promising overall attitude towards pharmacotherapy and medical genetics for smoking cessation. Psychotherapeutics combined with counseling could be one avenue to aid in cessation [33], as could providing in-patient treatments for smokers [34,35].

4. CONCLUSIONS

Despite the scarcity of smoking cessation aids in Indonesia, there is an overall open attitude towards medical genetics, pharmacotherapy, and medical consultation for cessation. With advancements, refinements, and a variety of combinatorial aids for pharmacotherapy and behavioral treatment protocols underway, implementation and feasibility testing suitable to Indonesians in various parts of the country could be done in a more structured and informed manner in the future.

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CONFLICT OF INTERESTS

The authors declare that there is no conflict of interests.

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