Socio-demographic, behavioral and mental-health factors associated with recreational laughing gas use: A cross-sectional study among adolescents in the Netherlands

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Abstract

Introduction: The recognition of laughing gas being a dangerous and increasingly used drug in many countries emphasized the need to identify high-risk groups in order to improve preventive approaches. Methods: In this cross-sectional study, a secondary data analysis was performed to explore the factors associated with laughing gas use and the degree of use within the group of laughing gas users. Binary logistic regression analyses were performed to assess the socio-demographic, behavioral and mental-health factors associated with laughing gas use. Results: The participants in the obtained data set included 11780 high school students between 12 and 18 years old from the Netherlands. This study showed that 6.2% of the sample ever used laughing gas in their life. Within the group of ever users, 72.2% used the drug on less than six days and 24.2% used the drug in the past month. Laughing gas use is associated with bullying behavior, the use of soft and hard drugs and having a low educational level. Discussion/conclusion: This study indicates that adolescents involved in bullying, using soft and hard drugs and having a low educational level have an increased risk of being a laughing gas ever user. Preventive approaches should therefore target these highrisk adolescents. Yet, further research is needed to establish causal relationships between the found associated variables and laughing gas. Additionally, the degree in which laughing gas is used simultaneously with other drugs should be investigated. For future interventions, a focus should be set on tackling the underlying problem of drug use and bullying in order to prevent both behaviors. Furthermore, interventions for laughing gas use should emphasize the danger of using laughing gas in combination with other drugs.

Introduction

Nitrous oxide, better known as laughing gas is a very popular and increasingly used recreational drug in several developed countries [1, 2]. Evidence from the Global Drug Survey 2015 showed that laughing gas is ranked as the 7th most popular drug in the world [3]. The percentage of participants who ever used laughing gas in their life was highest in the Netherlands (48%), followed by the United Kingdom (38%) and the United states (21%) [3]. The Dutch institute for mental health and addiction studied the recreational laughing gas use in the Netherlands over the past years. In 2013, 26% of the adolescents and young adults between 15-and 35 years old used laughing gas at least once in the past year. In 2016, this number already increased to 37%, which makes it the third most used drug in the Netherlands right after ecstasy and cannabis [4]. Laughing gas use is also already prevalent in a younger population. Research showed that in 2015, 8% of the high school students between 12 and 18 years old used laughing gas at least once in their life [1].

The use of laughing gas can lead to many adverse effects and short and long-term negative health problems [5]. Adverse effects are mostly experienced by heavy users and can include headache, nausea, confusion, numbness [6], dizziness, loss of balance and an impaired memory and cognition [7]. On the short term, laughing gas is very dangerous when it is combined with large amounts of alcohol since the narcotic effect of alcohol can lead to oxygen deficiency. Additionally, laughing gas is sometimes inhaled directly from the gas tank which can lead to freezing of the lips or lungs. When experiencing a cold, laughing gas increases the pressure in the head which can lead to ear pain or even hearing damage [5]. On the long term, evidence suggests that severe laughing gas use at young age can lead to underdevelopment of the brain and serious neurological disorders [8]. Finally, there are indications that laughing gas use leads to increased homocysteine levels in the blood and this

is a risk factor for cardiovascular diseases [8].

Up until recently, recreational laughing gas was very popular among adolescents because the drug is legal, cheap and very easily accessible [9]. However, due to many laughing gas related accidents in the past years [10], the Dutch government recently announced that there will be a ban on the sale of recreative laughing gas [11]. Apart from this ban, the government emphasizes the need for revision on prevention and information materials. This is necessary to inform and protect young people against the risks of laughing gas and to prevent illegal use [11]. Currently, preventive approaches for recreational laughing gas use aim to focus on adjusting the positive image of the drug among young users and by targeting the adolescents most at risk. This is done by informing them about the risks and explaining how to reduce these risks [12]. Following this approach, it is necessary to know who is exactly at risk and what factors are associated with the usage of laughing gas [12]. Researchers already gathered some information on user patterns and associated factors. Evidence suggests that laughing gas use is more prevalent among clubbers and the drug is mostly used in private house parties, followed by festivals, clubs and own homes [6]. Furthermore, specifically for high school students, laughing gas is more often used by males than females, mostly with an age of 17/18 years old living in the urban areas in the Netherlands. Additionally, it is known that laughing gas is often combined with alcohol, tobacco or cannabis [1, 9].

Evidence on other health-related factors contributing to the usage of laughing gas is lacking. However, more is known about the associated factors of adolescent substance use in general which might also apply for laughing gas users. Socio-demographic factors associated with adolescent substance use include family composition [13], educational level [14] and social economic status [15, 16]. Moreover, behavioral and social factors associated with adolescent substance use include sexual risk behavior [17, 18], bullying behavior [19-21], popularity [22], peer drug use [23] and parental relationships [23]. Additionally, mental health factors such as high levels of stress [24], poor resilience [25] and experiencing large impact life events [26] are known risk factors for adolescent substance use [21, 27, 28].

Given the above, there is already evidence on the factors associated with other drugs which should also be investigated specifically for laughing gas. It is important to gain insight in the associated factors in order to identify high-risk groups. With this information, future intervention and prevention programs for laughing gas use can be targeted to the adolescents most at risk and interventions can intervene on an appropriate level based on the associated factors. This high-risk approach has proven to be effective in the prevention of other recreational drugs [29]. For example, for cannabis use, prevention programs targeting vulnerable youth have been found effective in reducing recreational cannabis use. In these prevention programs, vulnerable youth was characterized by childhood adversity, behavioral difficulties, social disadvantage and adverse peer affiliation. Research on the associated factors was helpful for the identification of the high-risk groups and for improvement of interventions by intervening on the associated factors [28, 29]. Hence, most of the current prevention strategies for recreational cannabis use are based on these identified associated factors [30]. To improve the current preventive approaches regarding laughing gas, it is needed to gain insight into the associated factors of laughing gas use among Dutch adolescents. Therefore, the aim of this study is to investigate the socio-demographic, behavioral and mental-health factors associated with laughing gas use among high school students between 12- and 18 years old in the Netherlands.

Methods

Study design

In this quantitative study a cross-sectional design was used. Secondary data analysis was performed by using data from the adolescent health monitor 2019 in region West-Brabant. The adolescent health monitor is a nationwide survey which is carried out once in every 4 years. This is necessary because municipalities are obliged to map out the local health status at least once every 4 years according to the Public Health Act [31]. Therefore, most schools in the Netherlands were approached with the request to participate in the adolescent health monitor. For this survey, high school students between 12 and 18 years old completed a questionnaire about their health, well-being and lifestyle. The health monitor aims to gain insight into the health situation of this target group and municipalities can use these results to develop policies in order to promote the health and lifestyle of adolescents in the Netherlands [32]. For the original study, the data was gathered between September and December 2019. The Medical Ethics Review Committee of the AMC stated that the research does not fall within the scope of the Medical Research Involving Human Subjects Act and consequently does not require medical ethical testing [33]. For the current study, the secondary data analyses were performed between April and July 2020. This secondary study was ethically approved by the FHML research Ethics Committee under the license of the Master Health Education and Promotion.

Participants, recruitment and procedure

171192 high school students between 12 and 18 years old participated in the original study [33]. For the current study, the obtained data set included an unweighted sample in which only participants going to high school in West-Brabant were included. Recruitment for the original sample was done by approaching all school directors in the Netherlands with the request to participate in the study. Subsequently, information letters were sent to both students and their parents to inform them about the study. Participation was anonymous and entirely voluntary. Both the students and their parents had the right to refuse participation. The surveys were conducted digitally in the classrooms at the secondary schools and the students were allowed to fill in the questionnaire on a computer, laptop, tablet or smartphone.

Measurements

The regional adolescent health monitor survey contained 61 questions about several lifestyle themes. In this study, the answers from 20 questions were used to perform the data analysis.

The **dependent variables** in this study consisted of laughing gas ever use, the frequency of ever use and use in the past month. For the ever use, there was assessed if participants had ever used laughing gas in their life 0 (=no) and 1 (=yes). For these users, firstly the frequency of laughing gas use in the past month was assessed and recoded into use in the past month 0 (= no (never)) and 1 (=yes (one to two days; three to five days; six to nine days; > ten days)). Secondly, the frequency of ever use was assessed and recoded into 0 (=one to five days (one to two days; three to five days; more than ten days)).

For the **socio-demographic factors**, age was included. Literature showed that the average age adolescents start experimenting with drugs is 14 years old. Therefore, the variable 'age' was recoded into 1 (= \leq 14) and 2 (=>14) [9]. Furthermore for the sociodemographic factors, gender was assessed by 1 (= boy) and 2 (=girl) and educational level was assessed by 1 (= low: pre-vocational secondary school), 2 (=medium: higher general secondary education), 3 (= high: pre-university education) and 4 (=other education). Additionally, family composition was assessed and recoded into 1 (=living with both parents (living with both parents)), 2 (=co-parenting or living with 1 parent (with mother and her partner; with father and his partner; only with mother; only with father)) and 3 (= living by him/herself or with others(living by him/herself; living with others)). Also, the degree of

urbanization of the participants' place of residence was calculated by using postal codes and was recoded into three groups 1 (=strongly or very strongly urban (strongly urban; very strongly urban)), 2 (=moderately urban (moderately urban)) and 3 (=little or not urban (little urban; not urban)). Lastly, the variable 'perceived financial difficulties' was recoded into 1 (=perceives no financial difficulties (perceives no financial difficulties; perceives no financial difficulties but has to be careful)) and 2 (=perceives financial difficulties (perceives small financial difficulties; perceives large financial difficulties)).

For the behavioral factors, the number of times a participant was bullied at school in the past three months was assessed and recoded into bullying victimization 0 (=no (1 = never) and 1 (=yes (less than 2 times a month; 2 or 3 times a week; around once a week; multiple times a week)). In addition, the number of times a participant bullied someone else at school in the past three months was assessed and recoded into bullying perpetration 0 (=no (never) and 1 (=yes (less than two times a month; two or three times a week; around once a week; multiple times a week)). Additionally, for the behavioral factors, alcohol ever use was assessed and recoded into 0 (=no (only a few sips; no)) and 1 (=yes (yes, a whole glass or more)). Also, the frequency of alcohol use in the past month was assessed and recoded into alcohol use in the past month 0 (=no (never)) 1 (=yes (one or two days; three to five days; six to nine days; > ten days)). Furthermore, the ever use of weed and hash was assessed and recoded into a dichotomous variable 0 (=no (only a few sips; no)) 1 (=yes (yes, a whole glass or more)) and the frequency of use in the past month was assessed and recoded into weed/hash use in the past month 0 (=no (never)) 1 (=yes (one or two days; three to five days; six to nine days; > ten days)). Lastly, the ever use of one or more hard drugs including XTC, cocaine, mushrooms, amphetamines, LSD, GHB or heroine was assessed by 0 (=no) 1 (=yes).

For the mental health factors, resilience was assessed by eight indicating questions, recoded into a total score 0 (=insufficiently resilient) and 1 (=sufficiently resilient). The cutoff points for resilience were based on calculations made by the municipal health service. Additionally, stress was assessed by five indicating questions recoded into the combined variable 'often feeling stressed' 0 (=no) and 1 (=yes). If one or more of the five stress related questions were answered with 'yes', participants received the code 1. Furthermore, the experienced life events were assessed in which seven life events were taken into account including divorce of the parents, having a severe physical or psychological disease or someone in their family, addiction to alcohol, drugs or gambling of someone in their family and the loss of a family member. Since the loss of a family member was not correctly interpreted by the participants in the survey, this variable was excluded in the analyses. Furthermore, since divorce of the parents is more common and possibly less impacting than the remaining five life events, this concept was measured separately. Therefore, the divorce of the parents was assessed and recoded into 'experienced divorce of parents' 0 (=no (never experienced)) and 1 (= yes (has experienced; currently experiencing)). Additionally, for the remaining five high-impact life events there was assessed if respondents experienced one or more of these life events recoded into 'experienced one or more life events' 0 (=no (never experienced)) and 1 (= yes (has experienced; currently experiencing)).

Statistical analysis

For the data analysis, the statistical program IBM SPSS Statistics, version 24 for Windows was used. First, descriptive measures of frequencies were performed for all included variables to gain insight into the basic features of the sample. Secondly, the Pearson chi square was performed to assess the differences in independent variables between laughing gas ever users and never users, more frequent and less frequent users and last month users and non-last

month users significant at p < .05. Thirdly, a logistic regression analysis was performed in two steps. These two steps were performed separately for laughing gas ever use (0=no; 1=yes), the frequency of ever use (0=one to five days; 1=>six days) and the use in the past month (0=no; 1=yes). For the frequency of ever use and the use in the past month, only the ever users were taken into account. In step 1, a block-wise binary logistic regression analysis was performed to assess the association between laughing gas use (ever use, frequency of ever use and the use in the past month) and each group of independent variables (sociodemographic, behavioral and mental-health factors). The results were presented separately for each dependent variable in odds ratios with the corresponding confidence intervals (CI=95%). Additionally, the explained variance of each block was presented according to the Nagelkerke R^2 . In step 2, all factors significant at p < .05 in step 1 for at least one of the outcome measures (ever use, frequency of ever use and the use in the past month) were entered into the final multiple regression model. For the final model, a manual stepwise backward elimination method was used in which insignificant variables were filtered out at each step of the modelling until all variables were significant at p < .05. This was repeated for each outcome measure (ever use, frequency of ever use and the use in the past month) all using the same variables that were significant for at least one of the outcome measures in step 1. Again, odds ratios with the corresponding confidence intervals (CI=95%) and the explained variances (Nagelkerke R²) were presented for each outcome measure.

Results

Socio-demographic characteristics of the participants

A total of 11780 adolescents from 41 high schools were included in this study with a mean age of 14.27 (SD=1.26). The majority of the sample was female (50.3%), had a low educational level (51.4%), lived with both their parents (75.6%), perceived no or small

financial difficulties (96.0%) and lived in a strong or very strongly urban area (57.4%). Furthermore, only a small percentage of the participants reported to engage in bullying (4.1%) or were a victim of bullying (9.6%). With regard to substance use, approximately one third of the participants indicated to have ever used alcohol (36.2%). A smaller percentage of participants reported to have ever used weed/hash (8.0%) and an even smaller percentage reported to have ever used hard drugs (1.7%). A more complete overview of the sample is presented in Table 1.

| Independent variables | N (%) |
|--------------------------------------|--------------|
| Gender | 11529 |
| Male | 5732 (49.7) |
| Female | 5797 (50.3) |
| Age group | 11770 |
| ≤14 | 4589 (39.0) |
| > 14 | 7181 (61.0) |
| Educational level | 11733 |
| Pre-vocational secondary school | 6031 (51.4) |
| Higher general secondary education | 3103 (26.4) |
| Pre-university education | 2599 (22.2) |
| Family composition | 11761 |
| Living with both parents | 8894 (75.6) |
| Co-parenting or living with 1 parent | 1670 (14.2) |
| Living by him/herself or with others | 1197 (10.2) |
| Urbanization | 11780 |
| Strongly or very strongly urban | 6756 (57.4) |
| Moderately urban | 852 (7.2) |
| Little or no urban | 4172 (35.4) |
| Perceived financial difficulties | 11748 |
| Perceives no difficulties | 11277 (96.0) |
| Perceives difficulties | 471 (4.0) |
| Victim of bullying at school | 11512 |
| No | 10402 (90.4) |
| Yes | 1110 (9.6) |
| Perpetrator of bullying at school | 11523 |
| No | 11054 (95.6) |
| Yes | 469 (4.1) |
| Alcohol ever use | 11558 |
| No | 7378 (63.8) |
| Yes | 4180 (36.2) |
| Alcohol use in the past 4 weeks | 11035 |
| No | 7620 (69.1) |

Table 1: Description of the study sample

| Yes | 3415 (30.9) |
|---|--------------|
| Weed/Hash ever use | 11540 |
| No | 10618 (92.0) |
| Yes | 922 (8.0) |
| Weed/Hash use in the past 4 weeks | 11484 |
| No | 11071 (96.4) |
| Yes | 413 (3.6) |
| Hard drugs ever use | 11524 |
| No | 11324 (98.3) |
| Yes | 200 (1.7) |
| Resilience | 11687 |
| Insufficiently resilient | 1217 (10.4) |
| Sufficiently resilient | 10470 (89.6) |
| Often feeling stressed by 1 or more factors | 11628 |
| No | 6468 (55.6) |
| Yes | 5160 (44.4) |
| Divorce of the parents | 11637 |
| Never experienced | 8861 (76.1) |
| Experienced or experiencing right now | 2776 (23.9) |
| Experienced 1 or more high-impact life events | 11608 |
| Never experienced | 6660 (57.4) |
| Yes, experienced or experiencing right now | 4948 (42.6) |

Laughing gas use and the differences between user groups

Overall, 711 (6.2%) participants reported to have ever used laughing gas in their life. The relationship between laughing use and the included socio-demographic, behavioral and mental health factors is presented in Table 2. A significant relationship was found between laughing gas ever use and all socio-demographic variables. The percentage of men reporting to have ever used laughing gas was significantly higher compared to the percentage of women, X^2 (1, N=11285) = 4.21, p= .04. Also, the percentage of participants reporting to be older than fourteen, X^2 (1, N=11519)= 137.14, p=0.00, living in a strong or very strong urban area, X^2 (2, N=11529)= 6.19, p = 0.04, living by him/herself or with others, X^2 (2, N=11512)= 73.94, p=0.00, who perceived financial difficulties X^2 (1, N=11499)=43.87, p=0.00, and who had a low educational level X^2 (2, N=11482) =72.32, p= 0.00, was significantly more likely to report the ever use of laughing gas. For the mental health factors, the percentage of participants reporting to have experienced divorce of the parents, X^2 (1, N=11470)= 48.49,

p=0.00, to have experienced one or more high-impact life event, X^2 (1, N=11432)= 73.17, p=0.00, and who often experienced stress X^2 (1, N=11436)= 44.52, p=0.00 was significantly more likely to report the ever use of laughing gas. Moreover, for all behavioral factors apart from bullying victimization, a significant relationship was found with laughing gas ever use. The percentage of participants reporting the ever use of alcohol $X^2(1, N=11504)=639.59$, p=0.00, weed/hash $X^2(1, N=11504)=1625.7$, p=0.00 and hard drugs, $X^2(1, N=11492)=1012.77$, p=0.00 was significantly more likely to report the ever use of laughing gas. Furthermore, the percentage of participants reporting alcohol use in the past month $X^2(1, N=11448)=1146.58$, p=0.00 was significantly more likely to report the ever use of laughing gas. Moreover, the percentage of participants reporting to be a bullying perpetrator was significantly more likely to ever use laughing gas compared to the percentage of participants not reporting to be a bullying perpetrator $X^2(1, N=11487)=87.09, p=0.00$.

Within the group of ever users, 482 (72.2%) participants used laughing gas between one and five days in their life and 186 (27.8%) participants used the drug on six days or more. Furthermore, 154 (24.2%) participants within the group of ever users also used laughing gas in the past four weeks. The relationship between the included independent variables and the frequency of ever use and the use in the past month is presented in Table 2. Moreover, 1347 (11.7%) participants have been offered laughing gas at least once in their life. Laughing gas was mostly offered to the participants at home or at a friend's home (40.7%), on the streets (22.2%) or at a festival, concert or entertainment venue (24.4%).

| Independent variables | | Ever use | | Fre | quency of ever | Use in the past month | | | |
|--------------------------------------|---------------|----------------|----------------|------------------|-------------------|-----------------------|--------|-------|----------------|
| | Ever users | Never users | X ² | 1 till 5 days | 6 days or more | X ² | No | Yes | X ² |
| | N =702 | N= 10779 | | N= 477 | N=184 | | N= 481 | N=149 | |
| Gender, % | | | 4.21* | | | 3.29* | | | 6.58* |
| Male | 53.3 | 49.3 | | 50.6 | 55.8 | | 50.1 | 62.2 | |
| Female | 46.7 | 50.7 | | 49.4 | 44.2 | | 49.9 | 37.8 | |
| Age group, % | | | 137.14* | | | 149.78* | | | 0.00 |
| ≤14 | 18.2 | 40.3 | | 19.8 | 9.7 | | 18.0 | 18.2 | |
| > 14 | 81.8 | 59.7 | | 80.2 | 90.3 | | 82.0 | 81.8 | |
| Educational level, % | | | 72.32* | | | 71.1* | | | 4.64 |
| Pre-vocational secondary school | 65.5 | 50.3 | | 64.1 | 68.3 | | 62.4 | 70.5 | |
| Higher general secondary education | 23.0 | 26.8 | | 25.1 | 20.2 | | 26.0 | 17.4 | |
| Pre-university education | 11.5 | 23.0 | | 10.9 | 11.5 | | 11.6 | 12.1 | |
| Family composition, % | | | 73.94* | | | 73.80* | | | 1.14 |
| Living with both parents | 63.4 | 76.4 | | 65.8 | 57.5 | | 64.2 | 61.0 | |
| Co-parenting or living with 1 parent | 18.3 | 14.0 | | 17.4 | 21.0 | | 18.2 | 17.5 | |
| Living by him/herself or with others | 18.3 | 9.5 | | 16.8 | 21.5 | | 17.6 | 21.4 | |
| Urbanization, % | | | 6.19* | | | 8.76 | | | 0.46 |

Table 2: Relationship between the socio-demographic, behavioral and mental-health factors and laughing gas use

| Strongly or very strongly urban | 59.2 | 57.2 | | 60.0 | 59.1 | | 58.8 | 57.1 | |
|---|------|------|---------|------|------|----------|------|------|--------|
| Moderately urban | 4.9 | 7.4 | | 5.6 | 2.7 | | 4.6 | 5.8 | |
| Little or no urban | 35.9 | 35.4 | | 34.4 | 38.2 | | 36.6 | 37.0 | |
| Perceived financial difficulties % | | | 43.87* | | | 47.00* | | | 9.51* |
| Perceives no difficulties | 91.3 | 96.3 | | 93.1 | 87.6 | | 93.2 | 85.1 | |
| Perceives difficulties | 8.7 | 3.7 | | 6.9 | 12.4 | | 6.8 | 14.9 | |
| Victim of bullying at school, % | | | 0.201 | | | 10.632* | | | 25.33* |
| No | 89.2 | 90.4 | | 92.5 | 84.2 | | 92.7 | 78.1 | |
| Yes | 10.8 | 9.6 | | 7.5 | 15.8 | | 7.3 | 21.9 | |
| Perpetrator of bullying at school, % | | | 87.09* | | | 101.62* | | | 33.48* |
| No | 89.2 | 96.4 | | 91.4 | 83.7 | | 93.0 | 76.0 | |
| Yes | 10.8 | 3.6 | | 8.6 | 16.3 | | 7.0 | 24.0 | |
| Alcohol ever use (whole glass or more), % | | | 639.59* | | | 655.84* | | | 3.45 |
| No | 19.6 | 66.8 | | 21.8 | 8.6 | | 19.7 | 13.1 | |
| Yes | 80.4 | 33.2 | | 78.2 | 91.4 | | 80.3 | 86.9 | |
| Alcohol use in the past 4 weeks, % | | | 580.54* | | | 614.31* | | | 9.38* |
| No | 26.9 | 71.7 | | 28.7 | 14.8 | | 28.4 | 15.6 | |
| Yes | 73.1 | 28.3 | | 71.3 | 85.2 | | 71.6 | 84.4 | |
| Weed/Hash ever use, % | | | 1625.7* | | | 1731.73* | | | 37.30* |
| No | 52.1 | 94.6 | | 58.6 | 32.8 | | 57.5 | 29.2 | |
| | | | | | | | | | |

| Yes | 47.9 | 5.4 | | 41.4 | 67.2 | | 42.5 | 70.8 | |
|--|------|------|----------|------|------|----------|------|------|---------|
| Weed/Hash use in the past 4 weeks, % | | | 1146.58* | | | 1341.78* | | | 88.26 * |
| No | 73.1 | 97.9 | | 79.4 | 55.8 | | 81.9 | 42.8 | |
| Yes | 26.9 | 2.1 | | 20.6 | 44.2 | | 18.1 | 57.2 | |
| Hard drugs ever use, % | | | 1012.77* | | | 1260.63* | | | 45.45* |
| No | 83.1 | 99.3 | | 88.7 | 69.6 | | 88.4 | 64.7 | |
| Yes | 16.9 | 0.7 | | 11.3 | 30.4 | | 11.6 | 35.3 | |
| Resilience, % | | | 1.87 | | | 2.09 | | | 2.66 |
| Insufficiently resilient | 11.9 | 10.3 | | 10.9 | 13.5 | | 10.2 | 15.1 | |
| Sufficiently resilient | 88.1 | 89.7 | | 89.1 | 86.5 | | 89.8 | 84.9 | |
| Often feeling stressed by 1 or more factors, % | | | 44.52* | | | 42.64* | | | 0.00 |
| No | 43.5 | 56.4 | | 44.2 | 41.5 | | 43.3 | 43.1 | |
| Yes | 56.5 | 43.6 | | 55.8 | 58.5 | | 56.7 | 56.9 | |
| Divorce of the parents, % | | | 48.49* | | | 47.06* | | | 0.015 |
| Never experienced | 65.4 | 76.9 | | 67.0 | 61.6 | | 65.5 | 66.0 | |
| Experienced or currently experiencing | 34.6 | 23.1 | | 33.0 | 38.4 | | 34.5 | 34.0 | |
| Experienced 1 or more high- impact life events, % | | | 73.17* | | | 65.04* | | | 1.49 |
| Never experienced | 41.9 | 58.4 | | 43.8 | 39.3 | | 43.1 | 37.5 | |
| Experienced or currently experiencing | 58.1 | 41.6 | | 56.2 | 60.7 | | 56.9 | 62.5 | |

Note. * *p* < .05

Step 1

The full model containing all predictors was statistically significant, $X^2(7, N=11780)=789.98$, p=0.00. In the first block the explained variance was 6.2% (Nagelkerke R²) and this increased to 7.5% (Nagelkerke R²) in the second block after including the mental health factors. After adding the behavioral factors in the final block, the explained variance increased to 27.8% (Nagelkerke R²). Based on this final block, participants living in a moderately urban area (odds ratio [OR] = 0.41, confidence interval [CI] = 0.27-0.64) and participants with a high educational level (OR=0.59, CI= 0.44-0.78) were significantly less likely to report to be an ever user of laughing gas. Furthermore, participants who reported to be an ever user of alcohol (OR=2.93, CI=2.15-4.00), weed/hash (OR=3.49, CI=5.94) and hard drugs (OR=3.74, CI=2.54-5.51) were significantly more likely to have ever used laughing gas. Additionally, participants who used alcohol (OR=1.70, CI=1.29-2.23) or weed/hash (OR =1.25, CI =0.90-1.72) in the past month and participants who are bullying perpetrators (OR=2.07, CI=1.45-2.95) were significantly more likely to have ever used laughing gas. None of the mental health factors remained significant in the final model. A complete overview of the impact of each group of independent variables on the likelihood that participants have ever used laughing gas is presented in Table 3.

| Independent variables | Block 1 | | Block 2 | | Block 3 | |
|--|---------|--------------------------|---------------------------------|-------------|---------------------------------|-------------|
| | Nagelke | rke R ² 0.062 | Nagelkerke R ² 0.075 | | Nagelkerke R ² 0.278 | |
| | OR | 95% CI | OR | 95% CI | OR | 95% CI |
| Gender | | | | | | |
| Male ^a | | | | | | |
| Female | 0.95 | [0.80-1.12] | 0.86 | [0.72-1.02] | 1.03 | [0.85-1.25] |
| Age group | | | | | | |
| $\leq 14^{a}$ | | | | | | |
| >14 | 2.88* | [2.31-3.60] | 2.77* | [2.21-3.45] | 1.03 | [0.80-1.34] |
| Educational level | | | | | | |
| Pre-vocational secondary school ^a | | | | | | |
| Higher general secondary education | 0.81* | [0.66-0.98] | 0.79* | [0.64-0.96] | 0.84 | [0.67-1.05] |
| Pre-university education | 0.52* | [0.40-0.67] | 0.51 * | [0.39-0.66] | 0.59 * | [0.44-0.78] |
| Family composition | | | | | | |
| Living with both parents ^a | | | | | | |
| Co-parenting or living with 1 parent | 1.44* | [1.15-1.80] | 1.26 | [0.85-1.88] | 1.08 | [0.70-1.68] |
| Living by him/herself or with others | 1.83* | [1.45-2.33] | 1.64 * | [1.14-2.34] | 1.45 | [0.97-2.15] |
| Urbanization | | | | | | |
| Strongly or very strongly urban ^a | | | | | | |
| Moderately urban | 0.54 * | [036-0.81] | 0.52* | [0.35-0.79] | 0.41 * | [0.27-0.64] |
| Little or not urban | 1.00 | [0.84-1.20] | 1.01 | [0.85-1.21] | 0.93 | [0.76-1.14] |
| Perceived financial difficulties | | | | | | |

Table 2: Associations between the independent variables and laughing gas ever use in step 1 for each block

| Perceives no difficulties ^a | | | | | | |
|---|-------|-------------|-------|-------------|--------|-------------|
| Perceives difficulties | 1.63* | [1.17-2.26] | 1.39 | [0.10-1.93] | 1.00 | [0.67-1.50] |
| Resilience | | | | | | |
| Insufficiently resilient ^a | | | | | | |
| Sufficiently resilient | | | | | 1.03 | [0.76-1.40] |
| Often feeling stressed by 1 or more factors | | | 1.08 | [0.82-1.42] | | |
| No ^a | | | | | | |
| Yes | | | 1.54* | [1.28-1.84] | 1.15 | [0.95-1.41] |
| Divorce of the parents | | | | | | |
| No ^a | | | | | | |
| Yes | | | 1.04 | [0.73-1.49] | 0.98 | [0.66-1.45] |
| Experienced 1 or more high-impact life events | | | | | | |
| No ^a | | | | | | |
| Yes | | | 1.51* | [1.27-1.80] | 1.19 | [0.98-1.44] |
| Victim of bullying at school | | | | | | |
| No ^a | | | | | | |
| Yes | | | | | 0.73 | [0.52-1.04] |
| Perpetrator of bullying at school | | | | | | |
| No ^a | | | | | | |
| Yes | | | | | 2.07 * | [1.45-2.95] |
| Alcohol ever use | | | | | | |
| No ^a | | | | | | |
| Yes | | | | | 2.93* | [2.15-4.00] |
| Alcohol use in the past 4 weeks | | | | | | |

| No ^a | | |
|-----------------------------------|--------|-------------|
| Yes | 1.70 * | [1.29-2.23] |
| Weed/Hash ever use | | |
| No ^a | | |
| Yes | 4.55 * | [3.49-5.94] |
| Weed/Hash use in the past 4 weeks | | |
| No ^a | | |
| Yes | 1.25 | [0.90-1.72] |
| Hard drugs ever use | | |
| No ^a | | |
| Yes | 3.74 * | [2.54-5.51] |

^{*a*}*Reference category*

Within the group of ever uses, participants who reported to have ever used hard drugs (OR=1.89, CI =1.07-3.33) were significantly more frequent users of laughing gas (OR=1.89, CI=1.07-3.33). Additionally, within the group of ever users, participants who reported to have used weed/hash in the past month (OR=3.33, CI=1.73-6.40) and to be a victim of bullying (OR=2.23, CI=1.04-4.80) were significantly more likely to have used laughing gas in the past month. An overview of all factors associated with laughing gas use in the final model is presented in Table 4. The differences between the blocks for the frequency of ever use and the use in the past month are presented in the appendices.

| Independent variables | Ever users Nagelkerke R ² 0.278 | | Frequence | cy of ever use | Use in th | e past month |
|--|--|-------------|-----------|---------------------------------|-----------|---------------------------------|
| | | | Nagelke | Nagelkerke R ² 0.143 | | Nagelkerke R ² 0.216 |
| | OR | 95% CI | OR | 95% CI | OR | 95% CI |
| Gender | | | | | | |
| Male ^a | | | | | | |
| Female | 1.03 | [0.85-1.25] | 0.87 | [0.57-1.33] | 0.67 | [0.41-1.08] |
| Age group | | | | | | |
| $\leq 14^{\rm a}$ | | | | | | |
| > 14 | 1.03 | [0.80-1.34] | 1.70 | [0.83-3.49] | 0.94 | [0.45-1.93] |
| Educational level | | | | | | |
| Pre-vocational secondary school ^a | | | | | | |
| Higher general secondary education | 0.84 | [0.67-1.05] | 0.79 | [0.48-1.29] | 0.51* | [0.28-0.93] |
| Pre-university education | 0.59 * | [0.44-0.78] | 1.62 | [0.84-3.13] | 1.08 | [0.52-2.23] |
| Family composition | | | | | | |
| Living with both parents ^a | | | | | | |
| Co-parenting or living with 1 parent | 1.08 | [0.70-1.68] | 1.66 | [0.74-3.75] | 1.60 | [0.61-4.17] |
| Living by him/herself or with others | 1.45 | [0.97-2.15] | 1.50 | [0.75-3.02] | 1.04 | [0.46-2.33] |
| Urbanization | | | | | | |
| Strongly or very strongly urban ^a | | | | | | |
| Moderately urban | 0.41 * | [0.27-0.64] | 0.59 | [0.20-1.73] | 1.56 | [0.55-4.5] |
| Little or not urban | 0.93 | [0.76-1.14] | 1.15 | [0.75-1.75] | 1.06 | [0.65-1.71] |
| Perceived financial difficulties | | | | | | |
| Perceives no difficulties ^a | | | | | | |

Table 3: Associations between the independent variables and laughing gas ever use, frequency of ever use and use in the past month in step 1

| Perceives difficulties | 1.00 | [0.67-1.50] | 1.12 | [0.55-2.28] | 1.31 | [0.60-2.90] | |
|---|--------|-------------|------|-------------|-------|-------------|--|
| Resilience | | | | | | | |
| Insufficiently resilient ^a | | | | | | | |
| Sufficiently resilient | 1.03 | [0.76-1.40] | 0.86 | [0.45-1.63] | 1.07 | [0.52-2.20] | |
| Often feeling stressed by 1 or more factors | | | | | | | |
| No ^a | | | | | | | |
| Yes | 1.15 | [0.95-1.41] | 1.05 | [0.68-1.61] | 0.78 | [0.48-1.26] | |
| Divorce of the parents | | | | | | | |
| No ^a | | | | | | | |
| Yes | 0.98 | [0.66-1.45] | 0.81 | [0.40-1.64] | 0.50 | [0.22-1.14] | |
| Experienced 1 or more high-impact life events | | | | | | | |
| No ^a | | | | | | | |
| Yes | 1.19 | [0.98-1.44] | 1.01 | [0.66-1.56] | 0.98 | [0.60-1.61] | |
| Victim of bullying at school | | | | | | | |
| No ^a | | | | | | | |
| Yes | 0.73 | [0.52-1.04] | 1.99 | [0.96-4.15] | 2.23* | [1.04-4.80] | |
| Perpetrator of bullying at school | | | | | | | |
| No ^a | | | | | | | |
| Yes | 2.07 * | [1.45-2.95] | 1.27 | [0.65-2.47] | 1.95 | [0.99-3.85] | |
| Alcohol ever use | | | | | | | |
| No ^a | | | | | | | |
| Yes | 2.93* | [2.15-4.00] | 1.70 | [0.75-3.85] | 0.70 | [0.30-1.62] | |
| Alcohol use in the past 4 weeks | | | | | | | |
| NT a | | | | | | | |

No^a

| Yes | 1.70* | [1.29-2.23] | 1.15 | [0.62-2.14] | 2.03 | [0.99-4.14] |
|--|-------|-------------|-------|-------------|--------|-------------|
| Weed/Hash ever use | | | | | | |
| No ^a | | | | | | |
| Yes | 4.55* | [3.49-5.94] | 1.65 | [0.97-2.80] | 1.19 | [0.61-2.32] |
| Weed/Hash use in the past 4 weeks | | | | | | |
| No ^a | | | | | | |
| Yes | 1.25 | [0.90-1.72] | 1.11 | [0.63-1.95] | 3.33 * | [1.73-6.40] |
| Hard drugs ever use | | | | | | |
| No ^a | | | | | | |
| Yes | 3.74* | [2.54-5.51] | 1.89* | [1.07-3.33] | 1.34 | [0.71-2.51] |
| <i>Note.</i> $OR = odds$ ratio; $CI = confidence$ interval | | | | | | |

Note. OR = odds ratio; CI= confidence inter * p < .05 ^a Reference category

Step 2

In step 2, the variables significant in the final model of step 1 for at least one of the outcome measures were included in the final logistic regression analysis. For the ever use of laughing gas, the included variables were educational level, urbanization, alcohol ever use, weed/hash ever use, alcohol use in the past month, weed hash use in the past month, and bullying perpetration. For the frequency of ever use, only hard drugs ever use was included and for laughing gas use in the past month, the variables weed/hash use in the past month and bullying victimization were included. After the manual backward elimination procedure, the variables that remained significant are presented in Table 5.

Ever use

The final model for laughing gas ever use in step 2 was statistically significant, X^2 (8, N=11780) =1121.47, p=0.00, and the model explained 27.4% (Nagelkerke R²) of the variance in laughing gas ever use. Having a high (OR=0.57, CI=0.435-0.753) or medium (OR=0.79, CI=0.64-0.98) educational level was negatively associated with the ever use of laughing gas, indicating that participants with a high or medium educational level are less likely to be an ever user of laughing gas compared to participants with a low educational level. Furthermore, alcohol ever use (OR=2.92, CI=2.18-3.90), weed/hash ever use (OR=4 .65, CI= 3.61-6.01) and hard drugs ever use (OR=3.80, CI=2.64-5.45) appeared to be strong predictors of laughing gas ever use indicating that participants who ever used alcohol, weed/hash or hard drugs are more likely to be an ever user of laughing gas compared to participants who used weed/hash in the past month (OR=1.40, CI=1.03-1.92) and participants who used alcohol in the past month (OR=1.74, CI=1.34-2.26) are more likely to be an ever user of laughing gas. Participants being a perpetrator of bullying (OR=1.77, CI=1.27-2.47) are also more likely to be an ever user of laughing gas compared to participants who are not bullying perpetrators.

Frequency of ever use

The variables bullying victimization, alcohol ever use, weed/hash ever use, and hard drugs ever use remained significantly associated with the frequency of laughing gas ever use in the final model of step 2. The final model for the frequency of ever use was statistically significant, X^2 (4, N=11780) =60.77, p=0.00, and explained 12.8% (Nagelkerke R²) of the variance in the frequency of laughing gas ever use. Data showed that ever users who are victims of bullying (OR=2.09, CI=0.18-3.70) are more likely to frequently use laughing gas compared to ever users who are not a victim of bullying. Furthermore, ever users who also ever used alcohol (OR=2.11, CI=1.12-4.00), weed/hash (OR=2.01, CI=0.33-3.04) and hard drugs (OR=2.00, CI=1.25-3.20) are more likely to frequently use laughing gas compared to ever users who never used these drugs.

Use in the past month

The variables that remained significantly associated with laughing gas use in the past month in the final model of step 2 were bullying perpetration, bullying victimization and weed/hash use in the past month. The final model was statistically significant, X^2 (3, N=11780) =96.25, p=0.00, and the model explained 21.6% (Nagelkerke R²) of the variance in laughing gas use in the past month. Ever users being a perpetrator of bullying (OR=2.02, CI=1.10-3.70) and being a victim of bullying (OR=2.13, CI=1.15–3.97) are more likely to have used laughing gas in the past month. Moreover, ever users who used weed/hash in the past month (OR=5.18, CI=3.41-7.85) are more likely to have also used laughing gas in the past month.

| Independent variables | Eve | er users | Frequenc | y of ever use | Use in the past month | | |
|--|---------|--------------------------|----------|--------------------------|---------------------------------|---------------|--|
| | Nagelke | rke R ² 0.274 | Nagelker | rke R ² 0.128 | Nagelkerke R ² 0.216 | | |
| | OR | 95% CI | OR | 95% CI | OR | 95% CI | |
| Educational level | | | | | | | |
| Pre-vocational secondary school ^a | | | | | | | |
| Higher general secondary education | 0.79 * | [0.64-0.98] | | | | | |
| Pre-university education | 0.57 * | [0.44-0.75] | | | | | |
| Victim of bullying at school | | | | | | | |
| No ^a | | | | | | | |
| Yes | | | 2.09 * | [1.18-3.70] | 2.13 * | [1.15 - 3.97] | |
| Perpetrator of bullying at school | | | | | | | |
| No ^a | | | | | | | |
| Yes | 1.77* | [1.27-2.47] | | | 2.02 * | [1.10-3.70] | |
| Alcohol ever use | | | | | | | |
| No ^a | | | | | | | |
| Yes | 2.92 * | [2.18-3.90] | 2.11 * | [1.12-4.00] | | | |
| Alcohol use in the past 4 weeks | | | | | | | |
| No ^a | | | | | | | |
| Yes | 1.74 * | [1.33-2.26] | | | | | |
| Weed/Hash ever use | | | | | | | |
| No ^a | | | | | | | |

Table 4: Association between the independent variables and laughing gas ever use, frequency of ever use and use in the past month in step 2

| 4.65* | [3.61-6.01] | 2.01 * | [1.33-3.04] | | |
|--------|-------------|--------------------|--------------------|--------------------|--------------------------|
| | | | | | |
| | | | | | |
| 1.40 * | [1.03-1.92] | | | 5.18* | [3.41-7.85] |
| | | | | | |
| | | | | | |
| 3.80 * | [2.64-5.45] | 2.00 * | [1.25-3.20] | | |
| | 1.40 * | 1.40 * [1.03-1.92] | 1.40 * [1.03-1.92] | 1.40 * [1.03-1.92] | 1.40 * [1.03-1.92] 5.18* |

Note. OR = odds ratio; CI = confidence interval * p < .05^a Reference category

Discussion

The recognition of laughing gas being a dangerous and increasingly used drug in several developed countries emphasized the need to identify high-risk groups and to improve preventive approaches. The current study therefore explored the associations between laughing gas use and several socio-demographic, behavioral and mental-health factors. Additionally, further information was gathered on the degree of use within the group of users. Overall, there can be concluded that participants involved in bullying, using other soft and hard drugs and participants with a low educational level are more likely to use laughing gas.

The results of this study demonstrate that 6.2% of the high school students ever used laughing gas in their life. This is lower than expected since previous research in the Netherlands suggested an ever use of 8% among high school students [1]. This could be explained by the regional differences for drug use in the Netherlands since other drug use in region West-Brabant is known to be lower than the national average, which could also apply for laughing gas use [34]. Also, it should be considered that laughing gas use in the Netherlands is very high compared to other countries [3]. That is why it is likely that the ever use in other countries is lower than was found in the current study. Furthermore, the current study shows that within the group of ever users, 72.2% participants used laughing gas less than six times in their life, suggesting that most laughing gas uses the drug incidentally. An international study from 2015 confirms this suggestion by demonstrating that 58% of the participants used laughing gas only once or twice in their life [35].

This study adds to the current knowledge by demonstrating that bullying perpetration was positively associated with ever use of laughing gas and laughing gas use in the past month. No other studies reported this association before. However, it is known that bullies are more likely to use other drugs such as alcohol, tobacco and marijuana [19, 36-39]. Prior

research shows that bullying at a younger age increases the odds of reporting drug use at an older age, indicating a causal relationship between the two behaviors [40]. It is therefore logical that bullies are also more likely to use laughing gas. However, it remains unclear whether bullying is directly leading to adolescents to drug use or if mediating factors are involved [38, 41]. A study from 2007 suggested that the relationship between childhood aggression and adolescent substance use is potentially mediated since reactive and proactive aggression were indirectly associated with substance use through peer rejection and peer delinquency [38, 41]. Based on this suggestion, it could be possible that bullying perpetration in earlier age leads to laughing gas use at an older age, mediated by factors such as peer rejection. Bullying victimization, however, was only positively associated with laughing gas use in the past month meaning that ever users who are victims of bullying more often used laughing gas in the past month compared to ever users who are not victims of bullying. Again, no studies reported this association before although there is conflicting evidence on the link between bullying victimization and adolescent substance use in general. Some studies concluded that there is no elevated risk for substance use among bully victims [42, 43] whereas others studies did show that victims of bullying are more likely to engage in substance use, possibly to cope with rejection or to obtain a more positive social image [38, 44, 45]. Further research is necessary to establish the exact relationship between bullying perpetration, bullying victimization and laughing gas use.

Prior research showed that older high-school students are more likely to use laughing gas than younger high-school students [9]. In this study, no significant association was found between age and laughing gas use. This lack of association could be explained by the young sample in this study since only participants in the second and fourth grade of high school were included, resulting in a low mean age of 14.27 years old. Literature shows that laughing

gas use increases with age and is mostly used among 17/18-year-old high school students [9]. An association could possibly have occurred between age and laughing gas use if the mean age in the sample was higher. In addition, no significant association was found in this study between the degree of urbanization of the participants' place of residence and laughing gas use. However, previous research found that adolescents living in urban areas are more likely to use laughing gas compared to adolescents living in rural areas. According to literature, an explanation for this could be that there is recently an increase in rural drug use, not only in the Netherlands but also in other countries such as the United States [46, 47]. Drug use in rural areas is suggested to be increasing partly due to a lower educational level and informal social control in these areas, which could also apply for laughing gas use [46, 47]. Moreover, previous research suggested that adolescents with a poor mental health have an elevated risk to engage in substance use [21]. According to this evidence, adolescents who experienced high-impact life events, have a poor resilience and who experiences high levels of stress are more likely to use drugs [21, 26, 27, 48]. Against expectations, there was no significant association found in this study between resilience, stress and life events and laughing gas use. An explanation for this could be that laughing gas is more used as a recreative party drug whereas adolescents with mental health problems more often use drugs like marijuana, cigarettes or alcohol to ease the symptoms of their mental disorder or to cope with their emotions [27]. Therefore, a poor mental health may not be associated with laughing gas use, unlike the usage of other narcotic drugs.

In line with existing evidence, this study found that the use of soft and hard drugs is positively associated with laughing gas use [9]. The replication of these findings stresses the importance of soft and hard drugs in predicting laughing gas use. This study shows that students who ever used other soft and hard drugs and who used soft and hard drugs in the past

month were more likely to have ever used laughing gas. Within the group of laughing gas ever uses, participants who ever used other soft and hard drugs were more frequent laughing gas users and more often used laughing gas in the past month. These findings are in line with what was reported by a study from 2017 which demonstrated that laughing gas users often also have experience with using alcohol, tobacco and cannabis. Additionally, this study reported that laughing gas users often used alcohol, tobacco and cannabis before they started to use laughing gas for the first time [9]. This can be explained by the gateway theory which states that the use of a soft drug such as alcohol or tobacco can be a gateway to the use of heavier or more illicit drugs [49, 50]. For example, a study from Mayet et al showed that the use of alcohol and tobacco earlier in life increased the risk of cannabis initiation later in life [51]. This indicates that laughing gas ever use can be predicted by the ever use of soft drugs such as alcohol or weed earlier in life. A second explanation for the association between laughing gas use and other soft and hard drugs could be that laughing gas is used simultaneously with other drugs. A study from 2016 showed that laughing gas is regularly used in combination with other drugs such as alcohol, cannabis and sometimes even with hard drugs such as ecstasy, cocaine, amphetamine or ketamine [4]. The combined use of laughing gas should be avoided at all times since most drug related accidents result from mixing intoxications [2, 52]. In this study, it remains unclear whether participants used laughing gas simultaneously with other drugs or on separate days. Moreover, in line with literature, the current study showed that participants with a lower educational level are more likely to ever use laughing gas [9]. In previous research among high school students, a lower educational level was also found to be associated with the usage of other drugs such as tobacco, alcohol, cocaine, amphetamine, ecstasy [1]. Preventive approaches for laughing gas use as well as for other drugs should therefore focus on targeting low educated adolescents.

Strengths and limitations

The main strength of this study was the large sample size which provided the study with sufficient power to test several associations even though the group of laughing gas users was small with only 6% of the sample. Additionally, this study included variables that were not measured in previous studies on laughing gas, such as bullying behavior and mental health factors [9]. This helped identifying important contributing factors which may improve the preventive approaches for laughing gas use.

However, several limitations should be acknowledged in this study. At first, some factors suspected to be associated with laughing gas use could not be included in this study since they were not measured by the adolescent health monitor. While some of the included factors appeared to be very relevant, the contribution of the total set of factors was still limited with an explained variance of 28.7% indicating that other variables might have been involved. Variables suspected to be associated with laughing gas use include ethnicity, popularity [22], peer drug use [23] and parental relationships [23]. By adding these factors, the explained variance may increase.

Secondly, the self-reported survey increased the risk for social desirability bias. It is known that individuals tend to lie about sensitive questions such as drug use or other deviant behaviors because they want to answer desirably [53]. Adolescents might fill in that they have never used drugs while they actually have used drugs. Hereby, laughing gas use and the use of soft and hard drugs use could be underestimated. This bias could be limited in this study since the anonymity and digital administration of the survey is known to reduce the risk of social desirability bias [54]. However, there can still be assumed that the actual laughing gas and other drug use prevalence is higher than was found in the current study.

Thirdly, many variables were dichotomized in this study in order to have enough power and to sufficiently compare the results with data from previous adolescent health monitors. The health monitor is repeated every four years and trends in several behaviors such as drug use are hereby calculated according to dichotomized variables. As a consequence, the results for some variables were less specific than preferred. For example, for the outcome measure 'frequency of ever use', only the ever users of laughing gas were included which was 6% of the sample. To obtain enough power, this variable was dichotomized whereby only a distinction could be made between laughing gas use less than six days or more than six days. Literature shows that laughing gas is mostly used only once or twice [35] although this could not be confirmed in the current study. In addition, some other variables such as age and urbanization were recoded into fewer categories as well. Possibly, a significant association would have occurred for age and urbanization if these variables were not recoded into fewer categories.

Finally, it appeared that laughing gas users often also used other soft and hard drugs. However, in this study there could not be determined whether participants used these drugs at the same time or not. This is an important fact since the combination of laughing gas with other drugs is very dangerous [5, 52]. Therefore, this should be taken into account in future research.

Recommendations for future research and practice

In future research, the relationship between laughing gas use and other factors suspected to be associated should be explored since some of these factors were not included in the current study. For example, ethnicity should be included since evidence suggests that laughing gas is more often used among western individuals compared to non-western individuals [55]. Furthermore, it is possible that factors associated with other recreational

drugs, such as alcohol, tobacco and marijuana can also be associated with laughing gas use such as popularity [22], peer drug use [23] and parental relationships [23]. When the importance of these factors is confirmed, a clear overview can be formed on the factors predicting laughing gas use and this will help in further identifying the high-risk group. This might improve preventive approaches by specifically targeting the adolescents most at risk. Furthermore, a longitudinal study is warranted to establish a causal relationship between bullying behavior and laughing gas use as well as between soft and hard drugs use and laughing gas. As mentioned before, there can already be assumed that bullying at an earlier age probably leads to laughing gas use at a later age [41] and the usage of soft drugs is likely to cause the usage of laughing gas based on the gateway theory [49, 50]. Future interventions for bullying and drug use should focus more on the underlying problems of these behaviors. For example, skills training on how to cope with aggression or peer rejection could be a helpful approach for preventing both bullying and drug use. Moreover, since most laughing gas related accidents result from mixing intoxications, it should be investigated how often laughing gas is combined with other drugs nowadays and what factors determine the decision to combine these drugs among adolescents. It is of importance that future preventive approaches focus on reaching the high-risk groups and providing them with information about the dangers of combining laughing gas with other drugs.

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Appendices

Table A1: Association between the independent variables and the frequency of laughing gas ever use in step 1 for each block

| Independent variables | Block 1 | | Block 2 | | Block 3 | |
|--|---------|---------------------------------|---------|---------------------------------|---------|---------------------------------|
| | Nagelke | Nagelkerke R ² 0.050 | | Nagelkerke R ² 0.058 | | Nagelkerke R ² 0.143 |
| | OR | 95% CI | OR | 95% CI | OR | 95% CI |
| Gender | | | | | | |
| Male ^a | | | | | | |
| Female | 0.90 | [0.62-1.32] | 0.84 | [0.57-1.26] | 0.872 | [0.57-1.33] |
| Age group | | | | | | |
| $\leq 14^{a}$ | | | | | | |
| > 14 | 2.29* | [1.23-4.23] | 2.29 * | [1.23-4.24] | 1.70 | [0.83-3.49] |
| Educational level | | | | | | |
| Pre-vocational secondary school ^a | | | | | | |
| Higher general secondary education | 0.75 | [0.47-1.21] | 0.78 | [0.48-1.25] | 0.79 | [0.48-1.29] |
| Pre-university education | 1.29 | [0.69-2.42] | 1.31 | [0.69-2.46] | 1.62 | [0.84-3.13] |
| Family composition | | | | | | |
| Living with both parents ^a | | | | | | |
| Co-parenting or living with 1 parent | 1.46 | [0.87-2.35] | 1.81 | [0.82-3.99] | 1.66 | [0.74-3.75] |
| Living by him/herself or with others | 1.43 | [0.87-2.35] | 1.67 | [0.86-3.25] | 1.50 | [0.75-3.02] |
| Urbanization | | | | | | |
| Strongly or very strongly urban ^a | | | | | | |
| Moderately urban | 0.67 | [0.24-1.870 | 0.68 | [0.24-1.91] | 0.59 | [0.20-1.73] |

| Little or not urban | 1.17 | [0.78-1.74] | 1.18 | [0.79-1.76] | 1.15 | [0.75-1.75] |
|---|------|-------------|------|-------------|------|-------------|
| Perceived financial difficulties | | | | | | |
| Perceives no difficulties ^a | | | | | | |
| Perceives difficulties | 1.75 | [0.92-3.33] | 1.57 | [0.81-3.04] | 1.12 | [0.55-2.28] |
| Resilience | | | | | | |
| Insufficiently resilient ^a | | | | | | |
| Sufficiently resilient | | | 0.69 | [3.81-1.23] | 0.86 | [0.45-1.63] |
| Often feeling stressed by 1 or more factors | | | | | | |
| No ^a | | | | | | |
| Yes | | | 1.13 | [0.75-1.69] | 1.05 | [0.69-1.61] |
| Divorce of the parents | | | | | | |
| No ^a | | | | | | |
| Yes | | | 0.78 | [0.39-1.54] | 0.81 | [0.40-1.64] |
| Experienced 1 or more high-impact life events | | | | | | |
| No ^a | | | | | | |
| Yes | | | 1.21 | [0.81-1.82] | 1.01 | [0.66-1.56] |
| Victim of bullying at school | | | | | | |
| No ^a | | | | | | |
| Yes | | | | | 1.99 | [0.96-4.14] |
| Perpetrator of bullying at school | | | | | | |
| No ^a | | | | | | |
| Yes | | | | | 1.27 | [0.65-2.47] |
| Alcohol ever use | | | | | | |
| No ^a | | | | | | |

| Yes | 1.70 | [0.75-3.85] |
|-----------------------------------|-------|-------------|
| Alcohol use in the past 4 weeks | | |
| No ^a | | |
| Yes | 1.15 | [0.62-2.14] |
| Weed/Hash ever use | | |
| No ^a | | |
| Yes | 1.65 | [0.97-2.8] |
| Weed/Hash use in the past 4 weeks | | |
| No ^a | | |
| Yes | 1.11 | [0.63-1.95] |
| Hard drugs ever use | | |
| No ^a | | |
| Yes | 1.89* | [1.07-3.33] |

^a*Reference category*

Table A2: Association between the independent variables and laughing gas use in the past month step 1 for each block

| Independent variables |] | Block 1 | | Block 2 | | Block 3 | |
|-----------------------|---------|--------------------------|--|---------|---------------------------------|---------|--|
| | Nagelke | rke R ² 0.044 | e R ² 0.044 Nagelkerke R ² 0.058 | | Nagelkerke R ² 0.216 | | |
| | OR | 95% CI | OR | 95% CI | OR | 95% CI | |

Gender

Male^a

| Female | 0.59* | [0.39-0.90] | 0.58 * | [0.37-0.90] | 0.67 | [0.41-1.08] |
|--|--------|-------------|--------|-------------|-------|-------------|
| Age group | | | | | | |
| $\leq 14^{\rm a}$ | | | | | | |
| > 14 | 1.17 | [0.66-2.07] | 1.12 | [0.63-1.99] | 0.94 | [0.45-1.93] |
| Educational level | | | | | | |
| Pre-vocational secondary school ^a | | | | | | |
| Higher general secondary education | 0.59 | [0.35-1.01] | 0.58 | [0.34-1.01] | 0.51* | [0.28-0.93] |
| Pre-university education | 0.96 | [0.49-1.88] | 0.95 | [0.49-1.86] | 1.08 | [0.52-2.23] |
| Family composition | | | | | | |
| Living with both parents ^a | | | | | | |
| Co-parenting or living with 1 parent | 1.05 | [0.60-1.81] | 1.99 | [0.82-4.85] | 1.60 | [0.61-4.17] |
| Living by him/herself or with others | 0.97 | [0.55-1.70] | 1.15 | [0.72-3.13] | 1.04 | [0.46-2.33] |
| Urbanization | | | | | | |
| Strongly or very strongly urban ^a | | | | | | |
| Moderately urban | 1.45 | [0.57-3.71] | 1.47 | [0.57-3.81] | 1.56 | [0.55-4.5] |
| Little or not urban | 1.09 | [0.70-1.68] | 1.10 | [0.71-1.70] | 1.06 | [0.65-1.71] |
| Perceived financial difficulties | | | | | | |
| Perceives no difficulties ^a | | | | | | |
| Perceives difficulties | 2.09 * | [1.09-4.04] | 2.01* | [1.03-3.95] | 1.31 | [0.60-2.90] |
| Resilience | | | | | | |
| Insufficiently resilient ^a | | | | | | |
| Sufficiently resilient | | | 0.76 | [0.40-1.45] | 1.07 | [0.52-2.20] |
| Often feeling stressed by 1 or more factors | | | | | | |
| No ^a | | | | | | |

| Yes | 0.91 | [0.59-1.42] | 0.78 | [0.48-1.26] |
|---|------|-------------|-------|-------------|
| Divorce of the parents | | | | |
| No ^a | | | | |
| Yes | 0.48 | [0.22-1.04] | 0.50 | [0.22-1.14] |
| Experienced 1 or more high-impact life events | | | | |
| No ^a | | | | |
| Yes | 1.27 | [0.81-1.10] | 0.98 | [0.60-1.61] |
| Victim of bullying at school | | | | |
| No ^a | | | | |
| Yes | | | 2.23* | [1.04-4.80] |
| Perpetrator of bullying at school | | | | |
| No ^a | | | | |
| Yes | | | 1.95 | [0.99-3.85] |
| Alcohol ever use | | | | |
| No ^a | | | | |
| Yes | | | 0.70 | [0.30-1.62] |
| Alcohol use in the past 4 weeks | | | | |
| No ^a | | | | |
| Yes | | | 2.03 | [0.99-4.14] |
| Weed/Hash ever use | | | | |
| No ^a | | | | |
| Yes | | | 1.19 | [0.62-2.32] |
| Weed/Hash use in the past 4 weeks | | | | |
| No ^a | | | | |

No^a

| Yes | 3.33 * | [1.73-6.40] |
|--|--------|-------------|
| Hard drugs ever use | | |
| No ^a | | |
| Yes | 1.34 | [0.71-2.51] |
| Note $OR = odds$ ratio: $CI = confidence$ interval | | |

Note. OR = odds ratio; CI = confidence interval * p < .05^a Reference category