

Overcoming Health Risk of Down Syndrome Child with Obesity: Systematic Review

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Abstract: Down syndrome (DS) is a condition that occurs due to an abnormal number of chromosomes which is characterized by the presence of an additional chromosome. A child diagnosed with DS has three distinctive characters, namely having a low Intelligence Quotient (IQ), physical and mental limitations and having a weak immune system. Overweight and obesity are nutritional problems that often occur in people with DS, so it is necessary to study how the health risks that can be experienced by DS sufferers with obesity and how to overcome or minimize these risks. This Systematic Review study was conducted using the PubMed/Medline, Science Direct, and Google Scholar search databases. The search was limited to articles in peer-reviewed journals and literature reviews, which were written in English and Indonesian between 2012 and 2022. The study results showed that >40% of obesity occurred in children with DS. Obesity in people with DS can increase the risk of other health problems such as Obstructive Sleep Apnea (OSA) in adults with DS. In addition, dyslipidemia, hyperinsulinemia, NAFLD, Alzheimer's and tumors, and coronary heart disease are frequently reported in obese DS. Therefore, it is necessary to prevent nutritional problems by parents which includes parenting, feeding practices, and eating patterns. In addition, physical activity is needed for children with DS, especially for those who suffer from obesity. Fulfillment of nutrition and a healthy lifestyle throughout pregnancy is also needed to ensure the health of the child born and reduce the risk of having a baby with DS .

Keywords: Children with Down Syndrome, Down Syndrome with Obesity; Health Problems in Down Syndrome

INTRODUCTION

Down syndrome (DS) is a something conditions that occur consequence abnormality total tagged chromosome with existence chromosome additional. Individual with DS tend own disturbance mental and physical development . DS was first recognized in 1866 by Dr. John Longdon Down because its special features as relative height short, head shrunk, and a flat nose resembling Mongolians. Disorders that also include in condition disabled since born as mental retardation, difference physique certain as shape little face flat and rising a number of risk on condition medical including disturbance hearing loss hyroid disorder channel digestibility, and visual damage (Pramidi , Gartika , and Soewondo 2019). According to Nawawi, Gartika , and Soewondo (2018) children with DS other than experience mental and physical health disorders , also experience growth delayed teeth .

Refers to distraction chromosomes that occur in DS children, where occur advantage over more of the 350 genes on chromosome 21 that have three chromosomes (trisomy 21). Excess Chromosomes in people with DS change balance genetics body , resulting in change characteristics physique and ability intellectual , as well as disturbance in function physiology body . DS happened about 1 in 700 births baby and more often happened to mom pregnant over 35 years old (Pienaar 2012).

DS usually caused because failure in division cell or called nondisjunction . No is known why condition the could happen, however is known that failure in division cell this happens when fertilization and not related with what to do Mother During pregnancy. On condition this, trisomy 21 can occur not only during meiosis formation gametes but can also occur during early mitosis in development zygote. The primary oocyte that develops stopped at meiosis I prophase does not change in stage the until occur ovulation. Between time the oocyte experience nondisjunction. In DS, in meiosis I produces an ovum containing 21 autosomes and if fertilized by normal spermatozoa, which carry autosome 21, then formed zygote trisomy 21. Nondisjunction this could cause by several Thing as presence of viruses/ infections, radiation, and aging cell eggs. Enhancement age Mother influential to quality cell eggs . Cell egg will Becomes not enough good and at the time occur fertilization by spermatozoa, cells egg will experience error in cleavage . Besides that , in some study found existence hypothyroidism in children with DS included primary and transient hypothyroidism , pituitary-hypothalamic hypothyroidism , deficiency thyroxin binding globulin (TBG) and chronic lymphocytic thyroiditis . woman with age more from 35 years old more risky give birth DS babies compared with Mother age young (less than 35 years). The incidence of DS with age 35 year old mother , equal to 1 in 400 births . Whereas Mother with age not enough of 30 years , amounting to not enough than 1 in 1000 births. Change endocrine, such as increase androgen secretion, decreased rate hydroepiandrosterone , decreased systemic estradiol concentration , changes in concentration receptors hormones , and the hormones LH (Luteinizing Hormone) and FSH (Follicular Stimulating Hormone) which are suddenly increases when before and during menopause, can Upgrade possibility happening nondisjunction .

A diagnosed child have DS have three distinctive character that is own Low Intelligence Quotient (IQ), limitations by physique as well as mentally and have power stand weak body. Development and growth physique more DS children slow compared to normal child, accompanied by existence hypothyroidism, digestive problems, disorders heart congenital, and severe hypotonia, so that need done monitoring growth next (Aswara 2017). Swamilaksita et al . (2021) stated that overweight and obesity Becomes problem lots of nutrition occurs in people with DS. In publication is also mentioned a number of study related a lot case obesity that occurs in DS children with prevalence >40%. Esbensen (2010) explains that obesity own factor high risk for experience Obstructive Sleep Apnea (OSA) in adults with DS. because of that , study this will discuss how risk health that can experienced by people with DS with obesity and how get over it or minimize risk the .

METHOD

Study *Systematic Review* this done with using search database *PubMed/Medline, Science Direct and Google Scholar*. mostly journal used n the review came from from the *PubMed* database, where Relevant articles explaining risks health in obese DS sufferers and how to get over it identified use term searches for “ *obesity in down syndrome* ”, “ *health risk down syndrome with obesity* ””, and “ *strategy to reduce health risk in down syndrome with obesity* ”. Search restricted on articles in *peer-reviewed journals and literature review*, written in English and Indonesian between 20 12 and 2022. Publications older than 20 12 are not included for argumentation study . After literature obtained, then article filtered by title and abstracts, including filtering out irrelevant articles and duplications. The inclusion criteria used in this study are: (1) articles journal *peer review* original / main or results *review* literature, (2) room scope child *down syndrome* measured is the one who suffers obesity, (3) indicator for measure obesity and risk health defined with clear; (4) study done various countries; (5) written in language English or Indonesian; (6) articles foreign entry in scopus and domestic enter in Sinta. There are 195 articles generated from search, will but with all criteria applied

there are 16 articles fulfil condition for reviewed. Study list presented in **Table 1** , where is known based on the data that whole article good article *peer review* nor article *review* literature reveal that DS children are at risk tall suffer obesity with or without disease attendant other .

Table 1. Literature List

LITERATURE	LOCATION	TITLE	SAMPLE	METHOD	RESULTS
Yahiya <i>et al</i> (2012)	Egypt	<i>Leptin, insulin, and thyroid hormones in a cohort of Egyptian obese Down syndrome children: a comparative study</i>	36 children DS	Qualitative	Connection between hyperinsulinemia, disorders glucose fasting and obesity in DS children , which can make they risky more tall for suffer from the IRS. Also available enhancement median values of leptin and leptin-R in both OD and NOD groups with profile normal thyroid in lower children.
Gamere-Oosterom <i>et al</i> (2012)	Dutch	<i>Prevalence of Overweight in Dutch Children with Down Syndrome</i>	DS children born > 1982	Secondary Data July 2009 - February 2010	Prevalence rate excess weight between DS children with or without disturbance attendant no different by significant.
Real de Asua <i>et al</i> (2014)	Spanish	<i>A Cross-Sectional Study of the Phenotypes of Obesity and Insulin Resistance in Adults with Down Syndrome</i>	51 adults with DS living in the community and 51 controls healthy at the clinic take care Street House sick	Cross Sectional	adults _ with DS show prevalence excess high body weight and obesity. However, no find difference in lipid profile, prevalence insulin resistance, or syndrome metabolic between adults with DS and control .
Propst <i>et al</i> (2016)	Canada	<i>Midline Posterior Glossectomy and Lingual Tonsillectomy in Obese and Nonobese Children with Down Syndrome: Biomarkers for Success</i>	13 DS children aged 14 years who underwent MPG Plus LT	Qualitative	Obesity before or after operation indicates a better prognosis bad after MPG, show that initiative drop aggressive weight hould considered as addition for operation on population this.
Basil <i>et al</i> (2016)	United States	<i>Retrospective Study of Obesity in Children with Down Syndrome</i>	303 DS children aged 2 - 18 years	Cross Sectional	children with Down syndrome are at risk big for obesity and OSAS

LITERATURE	LOCATION	TITLE	SAMPLE	METHOD	RESULTS
Valentine <i>et al</i> (2017)	Italy	<i>Nonalcoholic Fatty Liver Disease in Italian Children with Down Syndrome: Prevalence and Correlation with Obesity-Related Features</i>	280 DS children (Age 8-15 yrs)	Cross Sectional	DS children with obesity showing risk for develop NAFLD from population pediatric general.
De la Piedra <i>et al</i> (2017)	Chile	<i>High frequency of dyslipidemia in children and adolescents with Down Syndrome</i>	DS children 2-18 years old	Cross Sectional	Lipid profile should be done more early on all patient with DS, regardless from existence factor risk dyslipidemia.
Nixon (2018)	United States	<i>Down Syndrome, Obesity, Alzheimer's Disease, and Cancer: A Brief Review and Hypothesis</i>	Article	Systematic Review	DS (trisomy 21), mixed complex from problem physical, mental, and biochemical, including enhancement risk Alzheimer 's disease and childhood leukemia, decreased risk of other tumors, and frequency of excess high weight / obesity .
Ruiz <i>et al</i> (2019)	Colorando	<i>Does Tonsillectomy Increase Obesity Risk in Children with Down Syndrome?</i>	78 DS patients	Analysis regression	No there is difference Among the most suitable %BMI curve in patients who saw OSA resolution after tonsillectomy vs patient with rest of OSA
Pitchford <i>et al</i> (2019)	Northern Ohio	<i>Diurnal cortisol and obesity in adolescents with and without Down syndrome</i>	32 teens with DS	Linear mixed model	DS children are at risk tall experience obesity and need intervention clinical.
Pierce <i>et al</i> (2019)	United States	<i>Trends in Obesity and Overweight in Oregon Children with Down Syndrome</i>	Record Medical (EMR)	Secondary Data	Children with Down 's syndrome has level more obesity all than population common, with risk tall especially for child female. mostly enhancement obesity occurs Among 2 and 6 years old

LITERATURE	LOCATION	TITLE	SAMPLE	METHOD	RESULTS
Paul <i>et al</i> (2019)	Africa	<i>The health benefits of exercise therapy for patients with Down syndrome: A systematic review</i>	Overview Systematic s and Meta-Analysis (PRISMA) , with focus on the period 2007-2018	Systematic Review	P bearer disabilities have a high risk of cardiometabolic and oxidative stress associated with increased insulin resistance, poor insulin sensitivity, atherosclerosis and hypertension
Magge <i>et al</i> (2019)	Philadelphia	<i>Cardiometabolic Risk and Body Composition in Youth With Down Syndrome</i>	150 DS teenagers (10-20 years old) and 103 teenagers non DS	Cross Sectional	Youth with DS have prevalence more dyslipidemia and prediabetes big than the usual teenager growing, which is not fully explained by VFA
Corona-Rivera <i>et al</i> (2019)	Western Mexico	<i>Maternal risk factors for congenital heart defects in infants with Down syndrome from Western Mexico</i>	Baby born with DS from January 2009 - June 2018	quantitative	Almost half from baby with DS in sample have CHD, being the most common ASD subtype and the rarest AVSD. Background behind ethnicity together with lack observed nutrition it seems contribute different in level CHD subtypes in DS patients.
Dierssen <i>et al</i> (2020)	Italy	<i>Down Syndrome Is a Metabolic Disease: Altered Insulin Signaling Mediates Peripheral and Brain Dysfunctions</i>	Article	Systematic Review	Disabled molecular this it seems Becomes reason height incident disturbance metabolism, diabetes and/ or obesity, as well as risk taller caught Alzheimer 's disease (AD) in DS.
Alghamdi <i>et al</i> (2021)	Arab	<i>Physical activity among children with down syndrome: maternal perception</i>	17 Children with DS	Descriptive	Obstacle activity physique for children with DS for designing customized intervention programs for Upgrade support and involvement children with DS to in activity physique by regularly.

RESULT AND DISCUSSION

Result(S)

Overweight and obesity is problem frequent nutrition reported occur during adolescence and early adulthood for people with DS (Swamilaksita *et al* 2021). Research conducted by Tershnjaku and Kadolli (2020) conducted on 95 people with DS aged 0-40 years showing that in children 0-18 years old as many as 47% have overweight nutritional status . Temporary that , research Rahmawati (2016) also shows as much as 40% of DS children experience obesity . Study other in Krause *et al* (2016) mentions the prevalence of overweight in DS adolescents

was 33.3% and the group the 3.21 times more risk big experience obesity than person with other disabilities.

Obesity is something condition, where occur excessive fat accumulation in body. Obesity is factor risk happening various type disease degenerative diseases, such as diabetes mellitus, hypertension, heart coronary and various type cancer. Besides that, obesity very related with problem psychosocial and burden social economics (Erviana & Hidayati 2019). Development trend obesity will cause burden economy in society. Trend the has shift than before occurs in low-income countries tall to income countries low. Overweight and obesity linked with more many deaths worldwide than lack weight. Globally there are more many people experience obesity than lack weight, thing this occurs in every region except parts of sub-Saharan Africa and Asia (Hsieh, Rimmer, & Heller 2014).

Based on research conducted by Gazizova *et al* (2012), prevalence obesity higher in people with disability intellectual than population general. The result in line with research that reports that there is trend enhancement prevalence excess weight in adults with disabled intellectual. In people with disabled intellectual enhancement obesity is a inequality Emerson and Hatton (2014). Intervention and education through gift promotion health hampered because cognitive, social, and behavioral adjustments with behavior in people with disabled intellectual as control self, determination goals, related skills _ with care health at home, perception risk and planning executive.

Erviana and Hidayati (2019) mention 6 factors risk obesity in people with DS, namely (1) poverty, (2) activity physical, (3) alcohol, (4) dietary habits and patterns eating, (5) environment the place stay, use drug, and (6) factor individual (type gender, age, education parents). Koritsas and Iacono (2016) revealed that compared with population general, more few people with disabled intellectual fulfil recommendation activity physical. Whereas intensity and frequency activity suitable physique _ could reduce risk disease heart coronary heart disease, stroke, osteoporosis, colon cancer, osteoarthritis, pain back down and increase mental health. According to Robertson *et al* (2014), the use of alcohol among people who experience disabled intellectual of course more a little compared with population in general. However found that level smoke far more many among teenager with disabled intellectual light. by significant consumption alcohol and tobacco no more big for woman however the opposite for men.

Environment the place Live could influence health people with DS, where is meant here is how and with who people with DS live, do together family, stay alone or live in the neighborhood House foster. Based on incident obesity found that people who live alone more tend for experience obesity compared with people who place stay together family or stay at home foster care (Koritsas and Iacono, 2016). People with DS who place stay together with family or in place foster own Settings more food tight, I mean in Thing pattern eat can be controlled by other people living with him compared with Live themselves (Koritsas & Iacono 2016). Besides it, Usage medicine is also one related factor with incident obesity as psychotropic used as drug antidepressants and drugs sleep. Use prolonged drug this has linked with addition weight and obesity in the population general.

Factor individual hold role in happening obesity in people with DS. According to type gender, prevalence incident obesity among woman more many compared men (Hsieh, Rimmer, & Heller 2014). That thing different with research conducted Tamin, Idris, Mansyur, & Syarif (2014) who explained in the research that prevalence obesity more tall among Men than woman. Based on level parental education, found that prevalence obesity highest namely in parents who have level education high. High parental education will improve social status economy family so that Upgrade power buy as well as consumption so that food consumed more a lot. That thing no in line with one research that suggests that poverty be one discussed factor in happening obesity in adolescents or mature with disabled intellectual because excess

nutrition has observed in developing countries and has been linked with fast change in the resulting diet from market modernization and globalization where food fast serve affordable and outlets that sell food solid and low-density nutrition many available (Hsieh, Rimmer, & Heller 2014). Inequality health experienced by people with disabled intellectual caused because condition those who are poor if linked with social economics (Robertson, Emerson, Baines, & Hatton 2014).

Problem obesity suffered by people with DS will Upgrade risk to problem other health . According to Esbensen (2010); Basil *et al* (2016); and Ruiz *et al* (2019), obesity own factor high risk for experience *Obstructive Sleep Apnea* (OSA) in adults with DS. In fact , some research (**Table 1**) mentions that obesity in people with DS can cause other health problems such as dyslipidemia (De la Piedra *et al* 2017), hyperinsulinemia (Yahiya *et al* 2012; Real de Asua *et al* 2014; Paul *et al* 2019; Magge *et al* 2019), NAFLD (Valentini *et al* 2017), Alzheimer's and Tumors (Nixon *et al* 2018; Dierssen *et al* 2020), and disease heart coronary (Corona-Rivera *et al* 2019). by detail Other possible Health risks arise because obesity in DS is presented in **Table 2**.

Table 2. Health Risks in Children with DS and How to Overcome Them

LITERATURE	HEALTH RISK	HOW TO OVERCOME
Yahiya <i>et al</i> (2012)	<ol style="list-style-type: none"> 1. obesity , 2. hypothyroidism , 3. decrease level metabolism 4. Diabetes mellitus 5. Hyperinsulinemia 	BB monitoring since early important because there is risk obesity is also affected genetics
Gamere-Oosterom <i>et al</i> (2012)	Obesity	Life structured healthy, including eat healthy food and do activity enough physique , will very effective in children with DS because trend they for follow tight routine
Real de Asua <i>et al</i> (2014)	<ol style="list-style-type: none"> 1. Upgrade CVD risk 2. Abdominal obesity 	Mediterranean Diet
Propst <i>et al</i> (2016)	Obstructive Sleep Apnea (OSA)	Midline posterior glossectomy and LT are beneficial in children with normal and overweight weight with DS who have OSA
Basil <i>et al</i> (2016)	<ol style="list-style-type: none"> 1. Obstructive Sleep Apnea (OSA) 2. Obesity 	Important for calculate BMI rather than depending on measurements heavy just moment evaluate healthy weight in children with Down 's syndrome (
Valentini <i>et al</i> (2017)	<ol style="list-style-type: none"> 1. Thyroid Disorders 2.NAFLD 3.Obesity 4. Cardiovascular risk (congenital) heart) 	by early followed by expert nutrition with monitoring strict weight.
De la Piedra <i>et al</i> (2017)	<ol style="list-style-type: none"> 1.Risk for dyslipidemia . 2.Risk of disease cardiovascular 	Recommend that screening dyslipidemia should done more early on all patient with DS, and that DS conditions should be considered as factor risk independent for development dyslipidemia .
Nixon (2018)	<ol style="list-style-type: none"> 1. Risk disease Alzheimer 2. Leukemia 	Leptin treatment reduces accumulation of beta amyloid in the brain, lowering cell toxicity nerves and, in cells nerve human, lower phosphorylated tau level

LITERATURE	HEALTH RISK	HOW TO OVERCOME
Ruiz <i>et al</i> (2019)	1. Obstructive Sleep Apnea (OSA) 2. Perioperative complications	To do tonsillectomy .
Pitchford <i>et al</i> (2019)	1. Cortisol dysfunction 2. Obesity	BB monitoring and upgrade activity physique
Pierce <i>et al</i> (2019)	1. OSA/sleep apnea 2. Hypothyroidism subclinical	Follow BMI percentile on the curve CDC growth (BB monitoring)
Paul <i>et al</i> (2019)	Risk cardiometabolic	Activity regular physical beneficial for increase VO2max and strength muscle. Besides that , activity regular physical reduce lipid peroxidation and damage Wall cell arteries , pathogenesis atheroma limited .
Magge <i>et al</i> (2019)	1. Dyslipidemia 2. Prediabetes	BB monitoring
Corona-Rivera <i>et al</i> (2019)	1. Atrioventricular septal defect (AVSD) 2. Disabled heart default	Fulfillment good nutrition at the same time pregnant as sour folate and Fe, have pattern good life as avoid cigarettes, caffeine , and alcohol throughout pregnant
Dierssen <i>et al</i> (2020)	1. Alzheimer 2. Diabetes 3. Decrease cognitive 4. Brain insulin resistance	Intranasal insulin administration has proven repair drop cognition in AD subjects and their effects even more good when insulin is given at stage beginning pathology (eg , MCI). Use drug antidiabetic including metformin and mimethi
Alghamdi <i>et al</i> (2021)	Obesity	Emphasize importance Upgrade awareness about need children with DS for activity physical infrastructure , in particular targeted programs supported by the government and the sector private

Data in **Table 2** explain how risk health other could suffered by children people with DS other than height risk obesity . As for the way get over it could see in the table that. A total of 12 literatures (75%) mention that monitoring weight need performed on DS children. Obesity normal occur because energy consumed bigger than issued, usually marked by BMI whose indicator is is weight and height according to age (for children). because of that care proper nutrition and pattern healthy life could made solution for reduce risk obesity so risk other diseases due to obesity can also avoided. Swamilaksita (2021) suggests that food that should be consumed in DS children such as food with a full menu containing carbohydrates, protein and vegetables as well as fruits could support grow flower and power stand body. Whereas food that should be avoided consist over 3 groups main that is food sweet , food fast (*junk food*) , and foods that contain gluten. DS children are also required always active activity and also increase cleanliness and safety in processing food as well as environment To use support health . More carry on explained by Bertapelli *et al* (2016) that prevention problem nutrition more for people with DS need noticed by parents . Parenting parents, practice gift food and pattern eat child is factor risks that affect nutritional status child. Mother's role in pattern nurturing child Becomes very important , especially in Thing intake eat . This thing related with limitations people with DS for prepare the food alone . parents _ more care with status child 's weight with DS than child who doesn't have DS, so will impact on change practice gift

eat child, like coercion for eat and give choice food to child . Perception parent could cause overweight in DS at age young.

Activity physique required for DS children , especially for those who suffer obesity . Rahmawati (2016) mentions that DS children have level activity physically inclined light so that risk obesity high (PAL = 1.44). Classification level activity physique based on the distinguished FAO/WHO/UNU (2001) be 3 levels in accordance with PAL (*Physical Activity Level*) value , i.e level activity low (PAL=1.4-1.69), moderate (1.7-1.99), and high (PAL=2-2.4). Study others also revealed similar thing _ that child with DS tend own activity low physical condition (Fauziyah and Wijatmadi 2019). Study the in line with research by Esposito *et al* (2012) which shows that that DS kids don't fulfil activity recommended physical , so that risky experience nutrition more. Activity low physique on the DS along with enhancement *sedentary lifestyle* and decline activity physique along with enhancement age. More carry-on Dam Fauziyah and Wijatmadi (2019) explained that activity child more many done inside House than outside home and tend choose activities that are not many needs motion, like listen music, playing gadgets, and watching tv. Will child for more many plays inside _ House no could be rejected by mother because condition child who doesn't accepted by friends his age when play outside home. Activity physique currently nor weight, such as running, sports (feather badminton, football, etc.), and playing active more many done when be at school. Whereas lesson sports at school only implemented for 2 hours per week so that Becomes limitation activity child. As a result, DS teenagers do not could activity currently nor heavy every day. Based on recommendation activity physique from *Australian National Physical Activity Guidelines, age teenager at least To do activity currently until heavy for 60 minutes every day* (The Department of Health 2017).

There is literature that explains that fulfillment good nutrition needed at the time pregnant as sour folate and Fe. Besides it's important for own pattern good life as avoid cigarettes, caffeine, and alcohol along pregnant. Pregnant women who have pattern life that doesn't good risky give birth child with DS (beside genetics) and babies born with DS at risk bring disabled born congenital (AVSD and disability heart congenital) (Corono -Rivera *et al* 2019). Things that are not lost important is guard health During pregnancy because condition Mother pregnant will determine condition baby born . Research conducted by Mundijo and Arsyad (2013) explains that there is correlation infection pregnancy with DS incident . Moment pregnancy takes place in get three mothers who come from from group mothers aged < 35 years . Third mother who has the DS child 2 people suffer from influenza and 1 person is infected rubella . rubella virus is one _ agent infections that are environmental teratogens that can influence embryogenesis and gene mutations so that cause change total nor structure the chromosomes that cause disability like DS.

CONCLUSION

Overweight and obesity is problem frequent nutrition reported occur during adolescence and early adulthood for with DS with presentation > 40%. Obesity in people with DS can Upgrade risk to problem other health like Obstructive Sleep Apnea (OSA) in adults with DS. Besides it, dyslipidemia, hyperinsulinemia, NAFLD, Alzheimer's and tumors, as well as disease heart coroner often reported suffered in DS with obesity. because of that , needed prevention problem nutrition by parents which includes pattern foster , practice gift food and pattern eat . Besides that, activity physique required for DS children, especially for those who suffer obesity. Fulfillment nutrition and pattern life healthy along pregnancy is also necessary for ensure health children born and reduce risk birth baby with DS.

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