Heatwaves and Preterm Births in Switzerland

Master Thesis

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Handed in by

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ABSTRACT

Recent evidence suggests that extreme temperatures can trigger preterm birth, which is the leading cause of infant mortality. Heatwaves are expected to increase with climate change in Switzerland, which could pose a great threat to human health, especially in vulnerable people such as pregnant women. The aim was to comprehensively assess if there is an increased risk for PTB during heatwaves in Switzerland and compare the effects using different definitions of heatwaves. This study looked into the short-term effects of heatwave exposure the last day of pregnancy. Moreover, a stratified analysis based on the age and nationality of pregnant mothers was also conducted. This study was done as an ecological study of time series, analysing almost 30'000 PTBs during summer months (June to August) from 2008 to 2016. Time-series analyses were done separately in each Swiss canton using a conditional quasi-Poisson regression model to estimate the association between heatwave and PTB risk. The model included one variable accounting for the pregnancies at risk of having a PTB, and another variable adjusting for the elevated PTB risk with gestational age. Two different types of heatwave definitions were analysed, one defined by air temperature only and another based on a heat index taking additionally into account the effects of relative humidity. Independent models were conducted for each definition, where the heatwave variable was included as a dummy variable. In total, seven different heatwave definitions were used, based on different combinations of thresholds (based on specific percentiles) on air temperature and heat index and duration in days. When pooling the canton-specific results, we found that PTB risk increased by 6% (CI: 0.96-1.17) and 2% (CI: 0.9-1.16) for heatwaves defined by the 90th temperature percentile, and 7% (CI: 0.92-1.25) and 8% (CI: 0.87-1.34) by the 95th temperature percentile for two and three days duration respectively. Meanwhile, the increase in risk was 2% (CI: 0.89-1.18), -6% (CI: 0.78-1.13) and 11% (CI: 0.91-1.36) when defining a heatwave by heat index ≥ 90 for two and three consecutive days, and by heat index ≥ 93 for two consecutive days, respectively. The increased risk was higher consistently in younger mothers (<31 years) and non-Swiss citizens.

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Abbreviations

CDC – Centres for Disease Control and Prevention
CI – Confidence interval
HI – Heat Index
JJA – June, July, August
NCCS - National Centre for Climate Service's
PTB – Preterm birth
RCP – Representative Concentration Pathway scenario
RR – Relative risk
WHO – World Health Organisation

Swiss cantons:
AG – Aargau
AI – Appenzell Innerhoden
AR – Appenzell Ausserhoden
BE – Bern
BL – Basel Landschaft
BS – Basel Stadt
FR - Fribourg
GE – Geneva
GL – Glarus
GR - Graübunden
JU – Jura
LU – Lucerne
NE – Neuchâtel
NW – Nidwalden
OW – Obwalden
SG – St. Gallen
SH - Schaffhausen
SO – Solothurn
SZ – Schwyz
TG – Thurgau
TI – Ticino
UR – Uri
VD – Vaud
VS – Valais
ZG – Zug
ZH – Zurich

1. Introduction

In today's changing climate, the frequency of extreme heatwaves are predicted to increase, which could pose a greater threat to human health, especially in vulnerable populations (Hoegh-Guldberg, 2018; Smith et al., 2014). It is estimated that in a world with 1.5°C warmer climate, 13.8% of the world's population will experience severe heatwaves every 5th year. Furthermore, if the temperature increases by 2°C, this number goes up to 36.9%, which is approximately 1.7 billion people (Dosio et al., 2018).

Different groups of people have been identified to be particularly vulnerable to heat. Among those particularly sensitive to heat stress according to Centres for Disease Control and Prevention (CDC) are: older adults (aged 65+), infants and children, people with chronic conditions, low income populations and outdoor workers to be (CDC, 2017). Moreover, pregnancy has been described as a period of increased vulnerability to climatic and environmental hazards, including heatwaves (Smith et al., 2014). In a study done in Spain, Arroyo and co-authors call heatwaves an acute stressor on pregnant women which puts this group particularly at risk to heatwaves (Arroyo et al., 2016). The susceptibility of a pregnant woman to temperature changes may be associated with extra physical and mental strain and greater risk of heat stress (Strand et al., 2011). Several studies have observed how extreme heat and heatwaves have short term effects on pregnant women with increased risk of preterm birth (PTB), among others health outcomes (Arroyo et al., 2016; Basu et al., 2010; Cox et al., 2016 Sun et al., 2019; Wang et al., 2013).

Worldwide, PTB is the leading cause of death before the age of 5 and it has been also associated with higher risk of diseases during the life of the preterm infant (World Health Organization [WHO], 2018). But many authors underline that there is uncertainty about the etiology of PTB, which is not entirely understood, and they urge researchers to do more studies on the topic (Chawanpaiboon et al., 2019; Räisänen et al., 2013; Walfisch et al., 2016; Wang et al., 2013). Furthermore, there is no universal definition of a heatwave (Rafferty, 2018), but the results from studies on heatwaves and PTB depend on how each study characterizes a heatwave (Ilango et al., 2020), the different methods to analyse the association (Kraemer, 2009) as well as the degree of vulnerability among regions (Levin 2003). Thus, further conclusive studies are needed.

This introduction aims to bring an overview of the current state of the art of the topic "heatwaves and preterm births" and highlight a research gap in the analysis of heatwaves effect on preterm births. It is composed of the following subsections: first, the current situation on climate change in Switzerland is described. Subsequently, essential concepts are defined, and the literature review gives background information on premature birth. Finally, this introductory section ends with a summary of the main topic "heatwaves and preterm births".

1.1 Climate change in Switzerland

According to the 2018 technical report written by the National Centre for Climate Service's (NCCS), Switzerland is a hotspot for changes toward hot temperature extremes (CH2018, 2018). Both heatwaves and extremely hot days are expected to increase in their frequency, intensity, and duration in Switzerland. Figure 1 is an excerpt from this technical report and shows the median change in extreme temperatures as a result of multiple climate models run with the highest Representative Concentration Pathway scenario (RCP8.5)(CH2018, 2018). The RCP8.5 scenario represents projected temperatures by year 2081-2100 without any effective emission mitigation policies (IPCC, 2019). The RCP8.5 scenario is commonly called the 'busines as usual' model. In today's climate, a *very hot day* is expected to happen approximately once per summer. In this RCP8.5 multi-model median, such an event is projected to increase to 2-4 days by 2035, to 6-11 days by 2060, and to 13-23 days by 2085, varying between regions. The NCCS technical report says that *very hot days* often occur together in a series of days, thus creating a heatwave (CH2018, 2018).

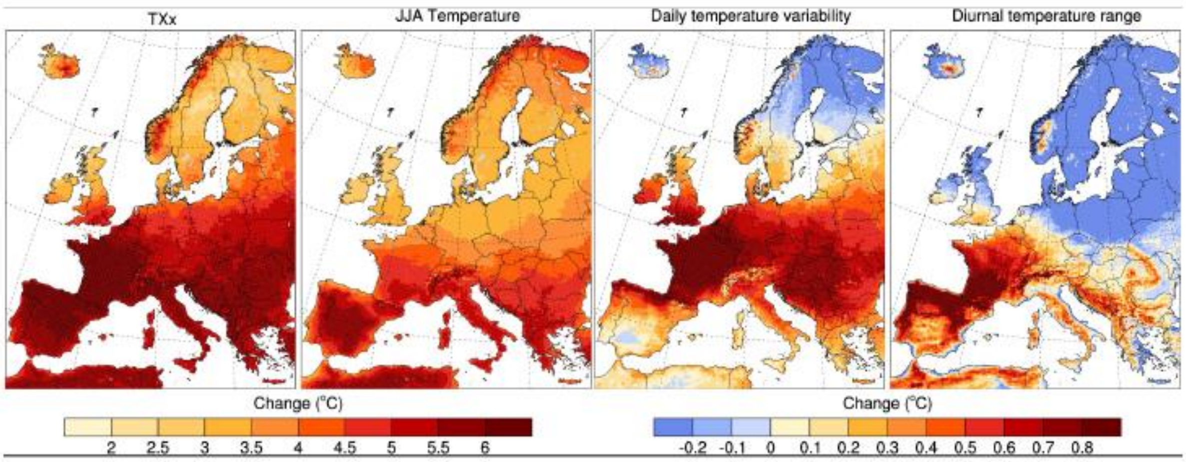

Figure 1.Multi-model median change in hot extremes (TXx), summer (June, July and August) mean temperature, daily summer temperature variability, and diurnal temperature range (DTR) by 2085 in (RCP8.5) with respect to present-day conditions (°C).

1.2 Definition of concepts

Current definitions of relevant concepts on the main topic of this Master thesis are shown below.

Preterm birth

According to the WHO, preterm birth (PTB) is defined as babies born alive before 37 weeks of pregnancy are completed, and depending on the gestational age, different categories can be distinguished: extremely preterm (<28 weeks), very preterm (28-32 weeks) and moderate to late preterm (32-37 weeks). In addition, according to the WHO complications from PTB are the leading cause of mortality in children globally under the age of 5, as well as many PTB babies suffer chronic disabilities (WHO, 2018). Meanwhile, it has been described that when looking at 184 countries, the PTB rate ranges from 5% to 18%, where 12% of all births on average are too early in lower-income countries, compared to 9% in higher-income countries. However, although there are several reasons why PTBs occur, the cause is often not identified (WHO, 2018).

Heatwaves

Currently, there is no a formal and standardized definition of a heatwave. However, some countries have adopted their own standards of definition (Rafferty, 2018). According to the *Encyclopædia Britannica*, the *Cambridge Dictionary*, and the *Merriam-Webster Dictionary*, a heatwave is a period of prolonged, abnormally high surface temperatures, relative to those temperatures normally expected (Rafferty, 2018; Cambridge Dictionary, n.d.; Merriam-Webster, n.d.). Meanwhile, the World Meteorological Organisation (WMO) defines a *heatwave* as a period of five consecutive days or more with a daily maximum temperature at least 5 °C above the average maximum temperature (Rafferty, 2018). MeteoSwiss, which is the Federal Office of Meteorology and Climatology, has its own definition of both *heat* and *heatwave* (MeteoSwiss, 2019), which are described below:

Heat = the perceived discomfort as a result of excessive air temperature.

Heatwave = a period of extreme heat stress, which can endanger human health.

Until 1st of June 2021, MeteoSwiss had a system of assessing the danger of a heatwave based on heat index (HI) by classifying it at different levels in order to publicly announce heat wave warnings (MeteoSwiss, 2021a). In this system, danger level 3 is classified as “significant danger”, danger level 4 as “severe danger”, and danger level 5 as “very severe danger”. However, danger level 5 is never issued as a warning in Switzerland as this kind of event is regarded as very unlikely to occur in these latitudes (MeteoSwiss, 2019). The description of measurement and prognostic values for danger levels 3 and 4 are as follows:

Danger level 3 (significant danger) – Heat Index $HI \geq 90$, with temperatures remaining over the threshold value for three days or more.

Danger level 4 (severe danger) – Heat Index HI ≥ 93, with temperature threshold remaining over the threshold value for five days or more.

Since 1st of June 2021 MeteoSwiss uses a different approach to warn for heatwaves. This system is based on daily mean temperature thresholds. MeteoSwiss calls this system more robust as it depends on temperature development both night and day, rather than high peaks in temperature (MeteoSwiss, 2021a). The description of measurement and prognostic values for danger levels 3 and 4 are as follows:

Danger level 3 (significant danger) – Daily mean temperature ≥ 25 °C for at least three consecutive days.

Danger level 4 (severe danger) – Daily mean temperature ≥ 27 °C for at least three consecutive days.

Heat Index

The heat index – also referred to as apparent temperature – is a way to measure the temperature experienced by combining the effect of actual air temperature and relative humidity. The HI is based on a direct relationship between actual air temperature and relative humidity (National oceanic and atmospheric administration [NOAA], n.d.). A Table of the Heat Index (HI) by MeteoSwiss is shown in Table 1 below. The HI is the apparent temperature in Fahrenheit (MeteoSwiss, 2019).

Table 1. Heat Index chart by MeteoSwiss. Relative humidity on the left and air temperature on top. The combination of relative humidity and air temperature makes the apparent temperature (HI) which is in Fahrenheit.

		Temperatur in °C											
		27	28	29	30	31	32	33	34	35	36	37	38
Relative Feuchtigkeit in %	30	79.6	80.8	82.2	83.8	85.5	87.5	89.6	91.9	94.4	97.1	100	103
	35	79.9	81.2	82.8	84.5	86.5	88.6	91	93.7	96.5	99.5	102.8	106.3
	40	80.4	81.8	82.5	85.4	87.6	90.1	92.8	95.8	99	102.5	106.2	110.2
	45	80.8	82.5	84.4	86.6	89.1	91.8	94.9	98.3	101.9	105.8	110	114.5
	50	81.4	83.2	85.4	87.9	90.7	93.9	97.3	101.1	105.2	109.6	114.4	119.5
	55	81.9	84.1	86.6	89.4	92.6	96.2	100.1	104.3	108.9	113.9	119.2	124.9
	60	82.5	85	87.9	91.9	94.7	98.7	103.1	107.9	113.1	118.6	124.6	130.9
	65	83.2	86.1	89.3	93	97.1	101.6	106.5	111.9	117.6	123.8	130.4	
	70	83.9	87.2	90.9	95.1	99.7	104.7	110.2	116.2	122.6	129.5		
	75	84.7	88.4	92.6	97.3	102.5	108.2	114.2	120.9	128			
	80	85.5	89.8	94.5	99.8	105.6	111.9	118.7	126				

1.3 Epidemiology – methods to study health outcomes in populations

Epidemiology can be defined as "the study of distribution and determinants of disorders in specified populations during a specific time period", where "distribution" concerns incidence or prevalence and "determinants" concerns risk factors (Kraemer, 2010). Different methods are used to analyse association and heterogeneity across populations. Three of the main study designs are cohort studies, case-control studies and cross-sectional studies. These study designs aim to evaluate associations between diseases and exposures by observing the strength of the relationship between exposure and the health outcome. The latter study design analyses the health outcome and exposure at one particular time point. Meanwhile, cohort and case-control studies measure health outcome occurrence and possible exposure associations over a period of time. Whereas a cohort study design divides the population into exposed and unexposed groups to later measure disease distribution which is favourable for rare exposures and can assess causality, the case-control design divides the population of interest into groups where the health outcome is observed and not observed, respectively. Thereafter, exposure distribution is studied in each group. The latter design is advantageous as multiple exposures and rare outcomes can be examined (Song & Chung, 2010). However, when studying the effects of geographical or temporal factors on disease incidence, an ecological study design is suitable. In this study design the unit of analysis is at population level, rather than individual level. This means using ecological variables characterising groups, organizations or places, and not data on characteristics of each person (Tu & Ko, 2008). Ecological study designs are particularly used when disease incidence is rare or if the study aim is to assess the association between population-level exposure to risk factors and disease. In addition, to evaluate the circumstantial effect on the population when exposed to risk factors (Levin, 2003).

1.4 Preterm birth

Prevalence

In a study which included data from 19 European countries, a wide variation in PTB trends was observed, however an overall increase in the number of early childbirths was detected (Zeitlin et al., 2013). In the US, Centres for Disease Control Prevention has documented increased number of PTB every year between 2014 to 2018 (CDC, 2019). However, studies show conflicting results with both upward and downward trends in PTB rates, and overall the prevalence of PTB in developed countries range between 4-13% (Walfisch et al., 2016; Räisänen et al., 2013). On average 12% of all births are too early in lower-income countries compared to 9% in higher-income countries (WHO, 2018). The PTB-rate was 7.5%in Switzerland 2008 (Federal Statistical Office [FSO], 2010), and 7.2% in 2015 (Euro Peristat, 2015). Figure 1 shows the estimated PTB rates worldwide in 2014 (Chawanpaiboon et al., 2019, Figure 1). The study by Chawanpaiboon et al., 2019 identifies a limitation in the data on PTB rates stating that the method of assessment of gestational age can affect the PTB rates, stressing that some older methods are not as accurate as newer ones (Chawanpaiboon et al., 2019).

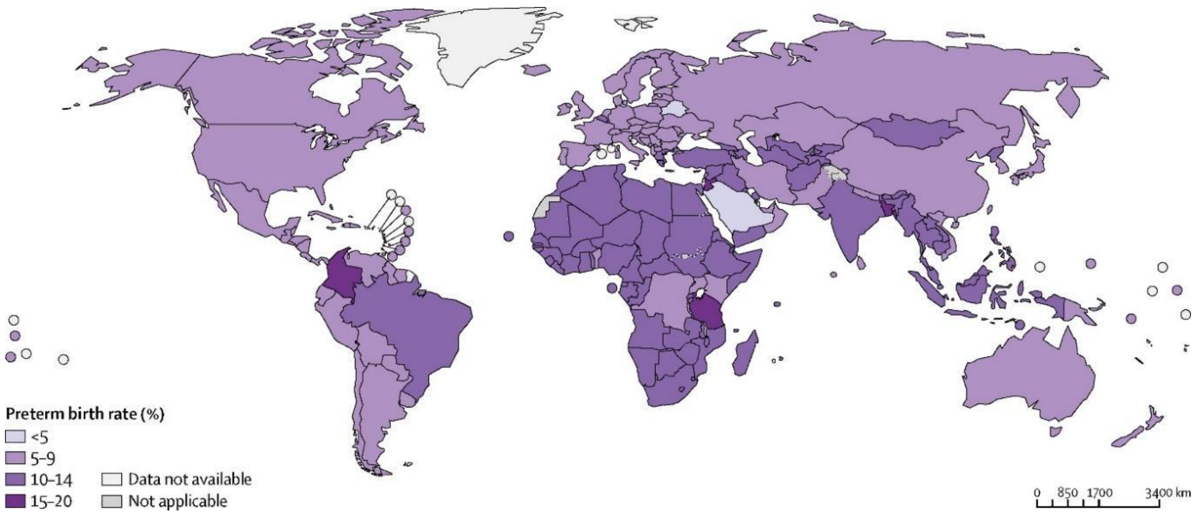

Figure 2. Estimated preterm birth rates 2014.

Etiology

Premature birth has been linked to multifactorial causes, involving both genetic, sociodemographic, behavioural, and environmental factors (Pennell et al., 2007; Zhu et al., 2008). The etiology behind the majority of PTBs is still unknown (Chawanpaiboon et al., 2019; Räisänen et al., 2013; Walfisch et al,. 2016). Although the effects of maternal heat exposure are not fully understood, there have been animal experiments and clinical trials investigating the biological mechanism. Animal studies have shown that heat stress can cause PTB; heat stress can cause hypersecretion of antidiuretic hormone and oxytocin, which can decrease uterine blood flow which shifts foetal metabolic pathways from anabolic to catabolic and result in PTB (Dreiling et al., 1991). Another study has found heat exposure might worsen physical burden and mental strain while being pregnant. That study clarifies, how pregnant women may be at greater risk of heat stress due to increases in internal heat linked to rise in fat deposition, weight gain and the growth and metabolic rate of the foetus (Strand et al., 2011).

Risk Factors

Several studies have identified particular factors including low socioeconomic status, overweight, age of the mother and ethnical group to increase the risk of PTB (Basu et al., 2010; McDonald et al., 2010; Räisänen et al., 2013; Smith et al., 2014). In a study conducted in Finland on the contribution of risk factors affecting PTB (not considering heatwave exposure), 1,390,742 singleton births were analysed. In that study, smoking was a key contributing factor explaining up to 33% of the variation in PTB cases between high and low socioeconomic status (SES) groups. Reproductive risk factors as placental abruption, placenta previa, major congenital anomaly, amniocentesis, chronic callus biopsy, anaemia, stillbirth, small for gestational age and foetal sex was the second most contributing factor and explained up to 25% of the variation between SES groups (Räisänen et al., 2013).

1.5 Heatwaves and PTB

Seasonality of PTB

It is important to separate seasonality in PTB and whether seasonal environmental factors have any association on PTB (Weinberg et al., 2015). Figure 1 shows that Bangladesh is one of the countries with the highest PTB rates, being in the 15-20% category. A seasonal variation in PTB rates has been identified in Bangladesh. This seasonal pattern shows lower incidences in the cooler time of the year, and a higher frequency in the pre-monsoon and monsoon seasons. This variational pattern implies that environmental factors have a triggering effect on PTB (Chawanpaiboon et al., 2019). Seasonal trends have also been seen in developed countries (Arroyo et al., 2015; Walfisch et al., 2016; Wells & Cole, 2002). Another study found a higher incidence rate of PTB in the summer period in the US (Walfisch et al., 2016). In contrast to the numerous studies finding increased PTB-rates during the warm season, when controlling for seasonal patterns in conception, studies find that the seasonal pattern in PTB-rates weakens. Because of seasonal patterns in conception, it is necessary to use a fetuses-at-risk approach when studying PTB, in order to avoid bias arising from seasonal patterns in conception (Weinberg et al., 2015).

High temperature exposure and perinatal health

Heat exposure has been associated with increases in the likelihood of adverse pregnancy outcomes (Chersich et al., 2020). The study by Walfisch et al., (2016) has found a significant linear relationship between heat stress and spontaneous early deliveries. Furthermore, the same study identifies maternal and foetal stress as one of the four major pathogenic causes resulting in early delivery. In addition, another study looking at 140 different populations in western- and developing countries, heat stress was proven to have a significant negative effect on birthweight in 108 populations, accounting for 9.6% of the in between-population variance after removing confounding factors (Wells & Cole, 2002). The same study indicates that infants with low birthweight have an increased risk of morbidity and mortality. To conclude, the study by Wells and Cole also stressed that expecting mothers are believed to be particularly at risk to heatwaves. In this context, over the last years there has been growing interest in the study of the link between high temperature exposure and PTB, and a notable number of studies have observed how exposure to extreme heat and heatwaves have short term effects on pregnant women and increase the risk of PTB (Arroyo et al., 2016; Basu et al., 2010; Cox et al., 2016 Sun et al., 2019; Vicedo-Cabrera et al., 2015; Wang et al., 2013).

A recent review compiling results from 36 different epidemiological studies on high temperature exposure and PTB, found that the evidence linking high temperature exposure and PTB was limited. The same study calls for more research on the topic, specifically more studies focusing on accurate estimation of temperature exposure and research on exact exposure windows (Zhang et al., 2017).

Also during heatwaves have PTB-rates been higher among tobacco users and certain ethnical groups in the US (Basu et al., 2017). Furthermore, when studying the effect on PTB when exposed to extreme heat, Cox et al. (2016) and Basu et al. (2017) have found a stronger association for underweight women compared to women who are overweight. Another study has found young mothers under the age of 20 to be at elevated risk when exposed to heatwaves (Basu et al., 2010). The same study found that mothers above 35 years of age had only a slight and nonsignificant elevated risk of having a PTB when exposed to a heatwave. In the latter study, maternal age is suspected to be a potential indicator of socioeconomic status, explaining their results. Furthermore, Basu et al. (2010) found no significant confounding effects by air pollutants, including carbon monoxide, sulphur dioxide and $PM_{2.5}$. Other studies highlight that extreme heat and air pollution are independently associated with increased risk of PTB (Wendee, 2020). Furthermore, results from another study show that the effect of heatwaves on PTB may be modified when combined with air pollution (Wang et al., 2020).

To the author’s knowledge, few studies have found an association between high temperature exposure and PTB in temperate climates. Research done in Belgium, Spain and Sweden have found that there might be an elevated risk for PTB when exposed to extremely high temperatures (Cox et al., 2016; Vicedo-Cabrera et al., 2014; Vicedo-Cabrera et al., 2015). On the other hand, research done in Germany and Canada found weak association or none (Auger et al., 2014; Wolf & Armstrong, 2012).

2. Study objective and research question

To the author's knowledge, no study has assessed the relationship between heatwaves and PTB in Switzerland to date. More research is needed to better understand whether pregnant women in Switzerland are vulnerable to heatwaves. This master thesis aims to offer an updated overview of the situation on PTB and hot summers in Switzerland. It also aims to identify any possible association between heatwaves and early deliveries by mothers. This information is important in order to improve current public health policies to protect pregnant women from heat and prevent additional health burden in the future due to climate change. In a changing Swiss climate with heatwaves expected to increase (CH2018, 2018), to identify vulnerable groups of people is of uttermost importance in order to be able to provide the best possible care for those at risk. From this standpoint, the following research questions are formulated:

Main research question: Is there an increased risk for PTB during heatwaves in Switzerland?

To answer this research question, different study objectives were raised:

- To explore the temporal evolution of PTB and heatwaves in Switzerland during 2008-2016
- To assess the effect of heatwave exposure on PTB using different definitions of heatwaves
- To analyse whether particular groups of women are at higher risk of delivering preterm when exposed to heatwaves assessing the influence of the age and nationality
- To evaluate if there are differences in the risk of PTB associated with heatwaves between cantons within Switzerland

3. Method

Switzerland is a country of central Europe divided into 26 cantons. This master thesis analyses daily birth and temperature data per canton in Switzerland during summer months June, July and August (JJA) from 2008 until 2016. The time period is set to nine years as changes in population structures are assumed to have stayed the same during this period, and information on gestational week was only available from 2008.

2.1 Study design

This study was done as an ecological study of time series to analyse PTB in relation to heatwaves. This ecological study was performed at population level, rather than at individual level, and is used to estimate associations between exposure and outcome, not causal links (Levin, 2003). Because the number of PTB-cases in the smaller cantons was very low, in this case, cantons with few births for statistical analyses were merged together with other cantons based on geographical proximity and weather similarities (see Figure 4).

2.2 Data

The following three data sets were used in this analysis; I) One data set containing daily mean temperatures per canton and II) another data set containing daily humidity and maximum temperature were used for heatwave analysis. III) The third data set used contained daily birth data for Switzerland. Weather data was obtained from MeteoSwiss, and birth data was obtained from the Federal Statistical Office in Switzerland. Each of the data sets used for analysis in this master thesis are explained in more detail below.

2.2.1 Mean temperature data

The data on daily mean temperatures used in this study was derived from a data set of 2*2 km gridded population-weighted average daily temperature per canton. This data has previously been derived by de Schrijver et al. (2021). First, hourly temperature observations were aggregated for each canton by day, creating daily mean averages for all grid cells throughout the cantons. Secondly, the data was population-weighted by using population maps. The population data is on municipality level for Switzerland and based on UN population maps from 2010 (UN WPP-Adjusted Population Count, v4.11 -2000) (Center for International Earth Science Information Network - CIESIN - Columbia University, 2018). de Schrijver et al. summed the total population living in each canton of Switzerland and additionally summed the population residing within each grid cell using Geographic Information System methods. Then, using the ratio between the population in the canton and per cell, population-weighted daily mean temperatures was computed for each cell. Finally, weighted-mean daily series for each canton was calculated from the temperatures of each cell and derived weight (de Schrijver et al., 2021).

2.2.2 Relative humidity and maximum temperature data

The data on daily mean relative humidity in this study rely on hourly observations from 34 Swiss monitor stations by IDAWEB (IDAWEB, n.d.), as no historical humidity observations on a small-scale grid is available in Switzerland. The data on daily maximum temperature comes from the same monitors. Bigger cantons were allocated more monitors than the smaller cantons. A 5-km buffer zone was applied around each station, and the monitors were weighted based on population density, again with the population maps from UN 2010 (UN WPP-Adjusted Population Count, v4.11 -2000) (Center for International Earth Science Information Network - CIESIN - Columbia University, 2018). Both the relative humidity and maximum temperature variable are therefore representing a mix of monitor stations within the same canton which have been weighted with the significant values based on population density.

For the heatwave analysis where relative humidity and maximum temperature were parameters included, 3 cantons had to be excluded completely due to missing relative humidity and maximum temperature data. These three cantons were *Uri + Obwalden + Glarus + Graübunden*, *Solothurn + Jura*, and *Aargau*.

2.2.3 Birth data

The birth data used in this study was provided by The Federal Statistical Office. It includes all live births in Switzerland from 2003 to 2019. The pool of births considered in this analysis was selected according to the following criteria (figure 3): i) births of mother resident in Switzerland, ii) births in Switzerland, iii) restricted to only singleton births, iv) only births with information on gestational week available, and finally v) births within the study period (January 2008- December 2016) was selected. The birth data includes both planned and unplanned Caesarion births. Moreover, the data includes daily information on total number of births, date of birth, number of PTBs and number of pregnancies at risk (gestational week 22<37), the nationality of the mother (Swiss/not Swiss citizenship) and age of the mother (below/above 31 years).

Due to missing PTB data in *Neuchâtel* and *Geneva*, these two cantons were excluded from 2008 in the analysis.

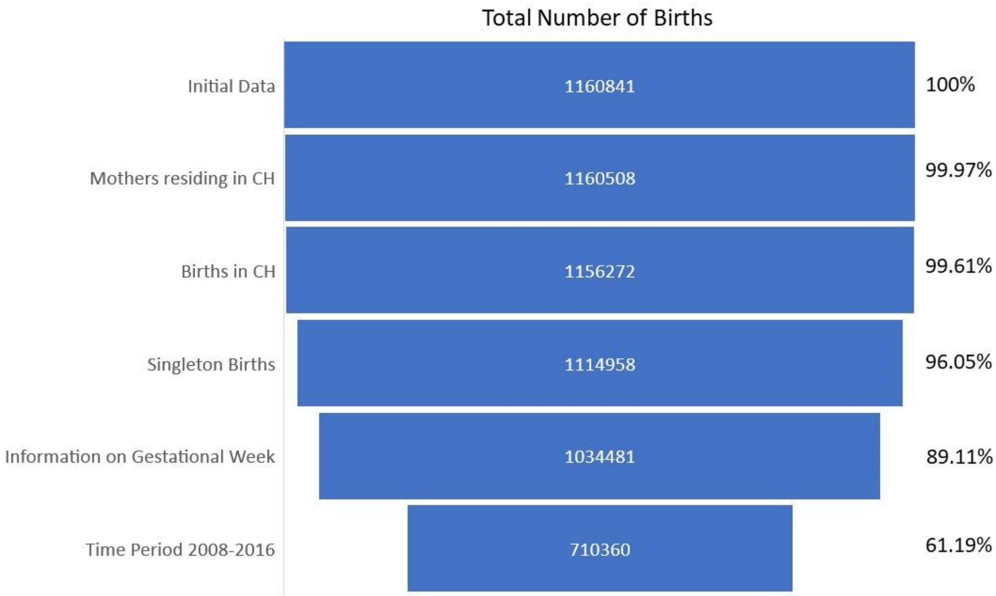

Figure 3. The steps in which the data on births was selected, showing the number of births in each step. After all criterions were selected 61.19% of the birth data was kept for further analysis.

2.3 Exposure classification

The exposure variable in this study is heatwave. To measure exposure, the heatwave phenomena must first be defined for this study. Because there is no formal definition of a heatwave that is universally agreed upon (WMO & WHO, 2015), this study uses two different types of heatwaves when studying exposure. The characterization of a heatwave can include air temperature, or HI (i.e. accounting for humidity), and the duration can differ. This study uses one definition that includes air temperature only and another which takes into account the effect of relative humidity. These two definitions are in line with the prior definition of MeteoSwiss which included HI, and the updated definition based on daily mean temperature (MeteoSwiss 2019; MeteoSwiss 2021a). This approach will enhance the chance of capturing all hot weather phenomena which could be associated with PTB. Exposure is assigned as a binary value (yes/no) to tell whether the mother experienced a heatwave the same day as giving birth. Heatwave exposure is determined by cantonal residence and heatwave events in each canton.

The first type of heatwave used in this study is based solely on air temperature and duration, and is defined by a daily mean temperature percentile and minimum duration thresholds. This type of definition based on daily mean temperature is in line with the new heatwave definition MeteoSwiss uses since 1st of June 2021 (MeteoSwiss, 2021a). In the descriptive analysis, the occurrence of this type of heatwave based on the 90th and 95th percentile, both for a minimum duration of two and three days, was explored. This heatwave definition with different thresholds was used for further time-series analysis comparing heatwaves and PTB. Other studies on heatwaves have defined heatwaves in a similar way, based on temperature cut-off percentiles and duration using multiple thresholds (Ilango et al., 2020).

The second type of heatwave defined in this study is based on HI, taking the effect of relative humidity in combination with air temperature into account. The HI was calculated based on maximum daily temperature and daily mean relative humidity, as done in previous studies (Mukherjee et al., 2021). Choosing a minimum of three consecutive days with HI ≥ 90 is aligned with the prior heatwave definition by MeteoSwiss (MeteoSwiss, 2021b). Furthermore, this study explored heatwaves defined by HI ≥ 90 for a minimum of two consecutive days (in order to obtain a higher number of events), and additionally, by HI ≥ 93 for a minimum of two consecutive days. A HI of 90 is equivalent to apparent temperature of approximately 32°C.

Table 2. The seven heatwave definitions based on different variables and thresholds used in this study.

Heatwave definitions

Heatwave type	Variables	Threshold	Duration (days)
1*	Tmean	90th percentile	2
		95th percentile	2
		90th percentile	3
		95th percentile	3
2**	Heat Index (Tmax & mean rel. Humidity)	HI ≥ 90	2
		HI ≥ 93	2
		HI ≥ 90	3

* In line with new heatwave definition by MeteoSwiss

** In line with prior heatwave definition by MeteoSwiss

2.4 Outcome measure

The aggregated number of PTB per day is the outcome variable. As defined by the WHO (2018), a PTB is measured as a live birth over 22 and before 37 weeks of gestation are completed. This was done per

Swiss canton. The daily number of PTBs was divided by the total number of on-going pregnancies at risk (between 22-37 gestational weeks). That is done in order to account for the underlying changes in risk due to seasonal patterns in conception (Vicedo-Cabrera et al., 2015). The analysis was also done for different sub-groups, in order to study whether particular groups of women are at higher risk when exposed to heatwaves. The sub-groups looked at in this study were nationality (Swiss/Not Swiss) and age (mothers below or above 31 years old).

2.5 Merging of cantons

As some less populous cantons are likely to have only a few cases of PTBs, these cantons were merged together with neighbouring cantons, for climatic reasons taking homogeneity in topography into account. A national map of how cantons were merged are shown in figure 4 below.

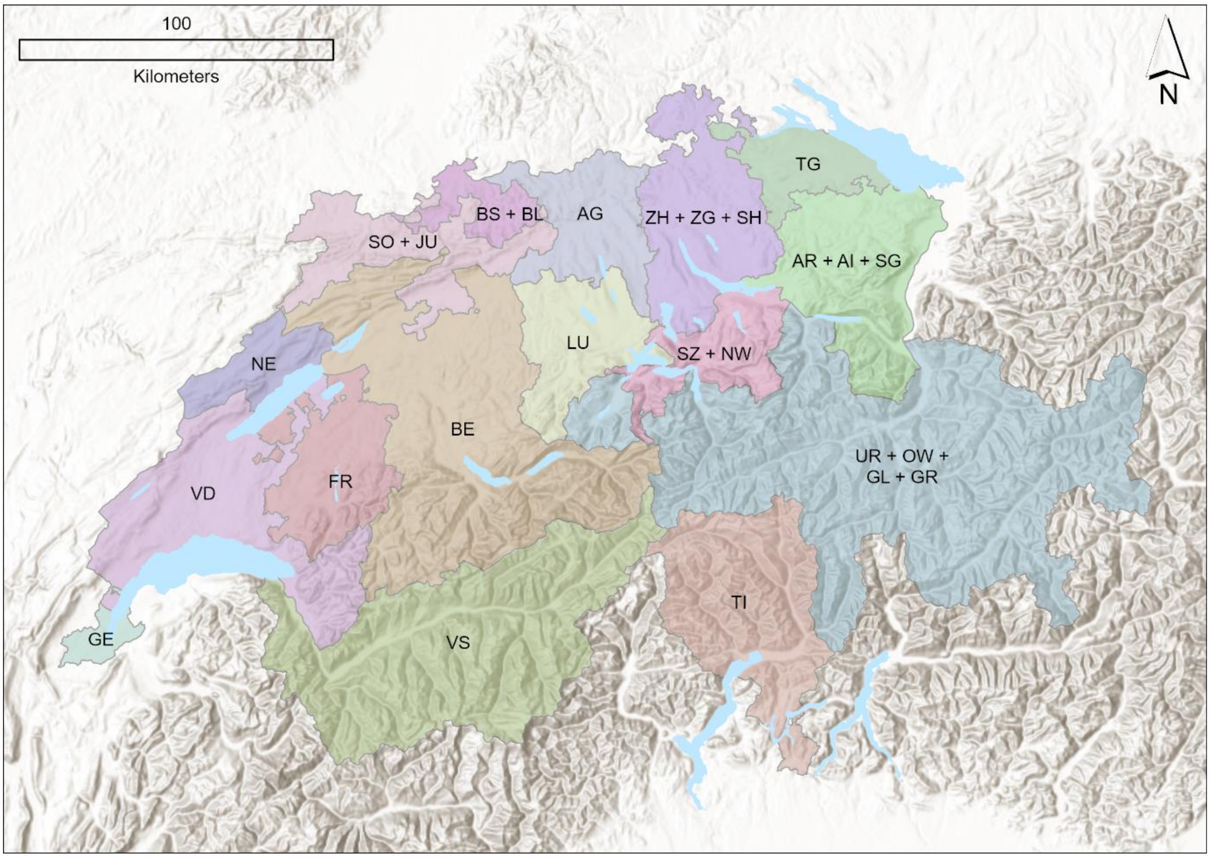

Figure 4. Switzerland's 26 cantons merged to a total of 16 canton clusters. Cantons were merged taking homogeneity in topography into account.

For the merged cantons, average mean temperature, maximum temperature and relative humidity between merged cantons was calculated. To reduce bias, the average value of each variable between merged cantons was calculated by taking into account the proportion of births in each of the merged cantons, and more weight was given to the temperature in cantons with more births. As an example, the first cluster of merged cantons includes Zürich, Zug, and Schaffhausen. Out of the total number of births based on these three cantons, 89% belong to Zürich. Therefore, the mean temperature in Zürich will be multiplied by 0.89, the mean temperature in Zug by 0.07 (7% of the births), and the mean temperature in Schaffhausen by 0.04 (4% of the births). Then all weighted average temperatures are added together, which finally gives us the weighted average temperature for this cluster. The relative humidity variable and maximum temperature variable was weighted in the same way as the mean temperature variable. Subsequently, this process was conducted for each cluster of merged cantons. Table 3 lists how cantons were merged and the weight of each canton.

Table 3. How cantons were merged and what weight is given to each canton based on number of births.

Cantons	Weight per canton
Zürich + Zug + Schaffhausen	0.89 + 0.07 + 0.04
Bern	1
Lucerne	1
Uri + Obwalden + Glarus + Graübunden	0.12 + 0.13 + 0.13 + 0.62
Schwyz + Nidwalden	0.80 + 0.20
Fribourg	1
Solothurn + Jura	0.78 + 0.22
Basel Stadt + Basel Landschaft	0.43 + 0.57
Appenzell Ausserhoden + Appenzell Innerhoden + St. Gallen	0.09 + 0.03 + 0.88
Aargau	1
Thurgau	1
Ticino	1
Vaud	1
Valais	1
Neuchâtel	1
Geneva	1

2.6 Statistical analysis

The statistical analysis was done in R Studio (version 1.4.1106). Time-series analyses were done in each merged canton separately, where PTB was the outcome and heatwave exposure was the independent variable. For the time series analysis, a conditional quasi-Poisson regression model was used to estimate the association between heatwaves and PTB risk. This was done for the summer season (June-July-August) between 2008 to 2016, and independent models were conducted for each definition of heatwaves and each canton. This kind of model accounts for overdispersion and provides an alternative to case-crossover analysis for a time series (Armstrong et al., 2014). In an ecological study as this one, ecological fallacy is a type of confounding which one has to be considered and adjust for. Ecological fallacy might occur when relationships observed in groups are presumed to also apply on individual level. In order to overcome ecological fallacy, regression analysis is recommended (Levin, 2003). Using a conditional Poisson regression model can control for confounding by including detailed stratification. The strata included in the model can be used to control for slow or regular changes in underlying risk (in this case e.g. pregnancies at risk) which might confound the results (Armstrong, 2014).

This study used a time-stratified approach to control for long-term and seasonal trend: each case day was matched with its control days according to the month and year within each specific canton, including a stratum variable in the conditional quasi-Poisson regression model. Strata with no cases of PTB were excluded from the analysis. Moreover, the day of the week was added as an explanatory variable in the model. Meanwhile, the heatwave indicator was included as a dummy variable for the same day of the birth. In addition, an offset was introduced in the model accounting for daily variations of pregnancies at risk (Vicedo-Cabrera et al., 2015). Because of seasonal patterns in conception, it is necessary to use a pregnancies-at-risk approach when studying PTB, in order to avoid bias arising from seasonal patterns in conception (Weinberg et al., 2015). Finally, the model adjusts for the daily distribution of the gestational age of pregnancies at risk, with the aim to give more weight based on the probability of giving birth conditional on the gestational age (the higher gestational age the greater the weight). As the probability of PTB increases with gestational age, this method adjusts for the odds of PTB that could influence short-term association estimates in this study (Darrow et al., 2009; Vicedo-Cabrera et al., 2015).

The association estimate between heatwave exposure and PTB was obtained in terms of relative risk (RR). The RR value expresses the change in risk of having a PTB when exposed to a heatwave, in comparison to not being exposed (CDC, 2012). The possible association between heatwaves and PTBs was analysed, not the causal link. First, time-series analyses were done in each merged canton separately. Then individual estimates were polled to estimate short term effects of heatwaves on PTB outcome on a national level using metanalytical techniques (meta regression) through the *mixmeta* package in R.

As the analysis was done per canton in Switzerland, this study will also allow for comparison in variability in PTB rates and exposure to heatwaves across the cantons. The possible factors modifying the vulnerability of pregnant women to heat are complex and range from physical, social, and biological.

The same time series analysis process was conducted individually for each subcategory of the mother to determine the influence of the nationality and age in association between heat and PTB risk per canton and in Switzerland as a whole.

A sensitivity analysis was conducted to validate the results. The sensitivity analysis was done for the total population as well as for all subcategories of mothers The same conditional quasi-Poisson regression model including the same outcome (PTB) and predictor variables (air temperature and HI), as well as explanatory variables (pregnancies-at-risk and daily changes in gestational week). In this step cantonal data was summarized to estimate short term effects of heatwaves on PTB outcome on a national level, again using metanalytical techniques (meta regression) through the *mixmeta* package in R. In the sensitivity analysis this step included a lag of up to three in order to investigate a possible exposure-response of up to 3 days before giving birth.

4. Results

This chapter presents the results found in this study on heatwaves and PTB in Switzerland. The study population corresponds to all singleton births (n = 710,360) in Switzerland from 2008 until 2016. Out of the study population, 4.2% (n = 29,831) were born preterm (before >37 gestational weeks).

4.1 Descriptive Analysis

The descriptive analysis is split into two parts: Heatwaves and Preterm birth. The sub categories below give an overview over heatwave and PTB occurrences in Switzerland between 2008-2016.

4.1.1 Heatwaves

Table 4 and 5 represent the total number of heatwaves per summer and canton based on two different types of heatwave definitions. As part of the descriptive analysis, different thresholds were examined for each type of heatwave.

In Table 4, heatwaves are based on daily mean temperature percentiles. They are defined by four different combinations of thresholds: by daily mean temperatures exceeding the 90^{th} and 95^{th} percentile and lasting for at least two and three consecutive days. In total, across all the cantons and years, 333, 159, 172 and 65 heatwaves occurred for the different definitions respectively. In Table 4, it is visible that 2013 and 2015 were exceptionally warm, with the most heatwaves in comparison to the other years studied. Table four also shows that it is more common to have temperatures above the 90^{th} percentile lasting for three days than above the 95^{th} percentile and two days. When looking at the results for one heatwave definition at the time, the number of heatwave events per year are similar between the cantons.

Table 4. Heatwave type 1, with 4 different combination of thresholds. The heatwaves are defined by daily mean temperatures above 90th and 95th percentile, for two and three days each. The number of heatwave events are shown per canton and summer (June to August).

Canton	2008				2009				2010				2011				2012				2013				2014				2015				2016				Total			
	*	**	***	****																																				
ZH+ZG+SH	1	0	0	0	1	0	0	0	2	0	1	0	2	1	1	0	2	0	1	0	4	2	2	2	1	1	1	0	7	4	5	3	2	1	1	0	22	9	12	5
BE	1	0	1	0	1	0	1	0	2	0	1	0	2	1	1	0	2	1	1	1	4	3	3	1	1	0	1	0	5	4	4	3	3	1	1	0	21	10	12	5
LU	1	1	1	0	1	0	0	0	2	0	1	0	2	1	1	0	3	1	1	0	3	2	3	1	1	0	1	0	7	3	5	2	3	1	1	0	23	9	12	3
UR+OB+GL+GR	0	0	0	0	1	1	0	0	1	1	1	0	2	1	1	0	2	2	2	1	4	2	3	2	1	0	1	0	6	3	4	2	2	2	1	0	19	12	12	5
SZ+NW	1	0	0	0	1	0	0	0	1	1	0	0	2	1	1	0	2	2	2	0	3	2	2	2	5	1	1	0	7	3	5	2	3	2	1	0	25	12	12	4
FR	1	0	0	0	1	1	1	0	2	0	1	0	2	1	1	0	2	1	1	1	4	3	2	1	1	0	0	0	5	3	4	2	2	1	1	0	20	10	10	4
SO+JU	1	0	0	0	1	0	0	0	2	0	1	0	2	1	1	0	3	1	1	1	4	2	3	1	1	0	1	0	6	4	5	2	3	2	1	0	23	10	11	4
BS+BL	1	0	0	0	1	0	0	0	2	1	1	0	2	1	1	0	3	1	1	1	4	2	3	1	2	1	1	0	6	3	4	2	3	1	2	0	24	10	11	4
AR+AI+SG	1	0	0	0	2	0	0	0	2	0	1	0	2	1	1	0	2	2	1	0	4	2	2	2	1	1	1	0	6	4	4	2	2	1	1	0	22	11	11	4
AG	1	0	0	0	1	0	0	0	2	1	1	0	2	1	1	0	2	0	1	0	5	2	4	1	1	1	1	0	7	4	5	3	2	1	1	0	23	10	11	4
TG	1	1	0	0	0	0	0	0	2	1	1	0	2	1	1	0	2	1	1	0	3	3	2	2	1	1	1	0	7	4	5	3	3	0	1	0	21	12	12	5
TI	0	0	0	0	1	0	0	0	2	2	1	0	1	1	1	0	1	2	2	1	2	2	2	1	1	0	0	0	4	3	3	3	2	0	0	0	14	10	8	5
VD	1	0	0	0	1	1	1	0	2	0	1	0	2	1	1	0	2	1	1	1	4	3	2	1	0	0	0	0	5	3	4	2	2	0	1	0	19	9	10	4
VS	1	0	1	0	1	1	1	0	1	0	1	0	2	2	1	0	3	2	2	1	3	1	3	1	2	0	0	0	5	2	4	2	3	2	1	0	21	10	12	4
NE	0	0	0	0	1	0	1	0	2	0	1	0	2	1	1	0	2	1	1	1	4	3	1	1	1	0	0	0	5	3	3	1	2	1	1	0	19	9	9	3
GE	0	0	0	0	2	0	1	0	1	1	1	0	3	1	0	0	2	0	1	0	3	1	1	0	0	0	0	0	4	3	3	2	2	0	1	0	17	6	7	2
Total	12	2	3	0	17	4	6	0	28	8	15	0	32	17	15	0	35	18	20	9	58	35	38	20	20	6	10	0	92	53	67	36	39	16	16	0	333	159	172	65

* Heatwave: temp ≥ 90th percentile, 2 days
** Heatwave: temp ≥ 95th percentile, 2 days
*** Heatwave: temp ≥ 90th percentile, 3 days
**** Heatwave: temp ≥ 95th percentile, 3 days

Table 5 shows the number of heatwave events for the type of heatwave defined by HI. Three different combinations of thresholds are used: both the HI reaches 90 or higher for at least two and three days in a row, as well as HI reaches 93 or higher for at least two days in a row. In Uri canton, data on maximum temperature is missing, therefore, this canton cluster is excluded from analysis. In the cantons of Solothurn and Aargau, data on relative humidity is missing, therefore these canton clusters are also excluded.

Table 5 shows that 134, 77 and 57 heatwaves occurred in total across all cantons and years for the different thresholds respectively. Particularly, *Basel Stadt + Basel Landschaft*, *Valais* and *Geneva* cantons have more heatwaves than the other cantons when defining heatwaves by HI. In general, the definition using HI 93 or higher for two consecutive days, is more common than the definition using a lower HI of 90 for three consecutive days. According to what is observed in Table 5 *Schwyz + Nidwalden* cantons experienced no heatwaves at all during the nine years. In *Appenzell Ausserhoden + Appenzell Innerhoden + St. Gallen* cantons only once did the HI reach 90 for two consecutive days in 2015, while no heatwave occurred there when using the other two definitions.

Table 5. Heatwave type 2, based on Heat Index (HI) and three different combination of thresholds. The heatwaves are defined by HI thresholds 90 ≥ for two and three days, as well as HI ≥ 93 for two days. The HI is based on daily maximum temperature and relative humidity. The number of events are shown per canton and summer (June to August).

Canton	2008			2009			2010			2011			2012			2013			2014			2015			2016			Total		
	*	**	***																											
ZH+ZG+SH	0	0	0	1	0	0	0	0	0	2	0	0	1	0	0	2	2	1	1	0	1	5	3	1	1	0	0	13	5	2
BE	0	0	0	1	1	0	1	0	0	1	0	0	1	1	0	1	0	0	0	0	0	3	4	1	1	0	0	9	6	1
LU	0	0	0	0	0	0	0	0	0	1	0	0	1	0	0	2	2	1	1	0	1	4	2	1	1	0	0	10	4	2
UR+OB+GL+GR																														
SZ+NW	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
FR	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	4	2	1	0	0	0	6	3	1
SO+JU																														
BS+BL	0	0	0	1	1	0	2	1	1	2	2	1	2	1	1	4	2	1	2	2	1	6	5	3	3	1	1	22	15	8
AR+AI+SG	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	1	0	0
AG																														
TG	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	1	0	0	0	0	4	1	1	0	0	0	6	2	1
TI	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	2	0	2	0	0	0	2	1	3	0	0	0	6	3	7
VD	0	0	0	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	4	3	2	0	0	0	6	3	2
VS	2	0	0	1	2	1	2	1	2	2	2	1	3	3	3	4	2	3	2	2	2	8	5	6	5	3	4	29	20	20
NE	0	0	0	1	0	0	1	0	0	0	0	0	0	0	0	1	0	0	0	0	0	4	4	3	0	0	0	7	4	3
GE	0	0	0	1	1	1	3	2	1	2	2	1	3	1	1	3	1	1	1	0	0	5	4	4	1	1	1	19	12	10
Total	2	0	0	8	6	2	10	4	4	11	7	4	12	7	6	22	10	9	7	4	5	50	34	26	12	5	6	134	77	57

* Heatwave: HI ≥ 90, 2 days
** Heatwave: HI ≥ 93, 2 days
*** Heatwave: HI ≥ 90, 3 days

When comparing the numbers in Table 4 and Table 5, it is evident that the heatwaves defined by temperature percentiles are more frequent than the heatwaves defined by HI. Similar to Table 4, the most heatwaves also occur in 2013 and 2015 in Table 5 This indicates that those were extremely hot summers.

Figure 5 below shows the total number of heatwaves per summer for all the Swiss cantons. It is evident that the summers of 2013 and 2015 were abnormally hot, independently of what heatwave definition is chosen. The heatwaves defined by daily mean temperature percentiles are coloured in red/brown palette, and the heatwaves based on HI are indicated in range of blue colour. The heatwaves based on daily mean temperature percentiles are in general more frequent than the heatwaves based on HI. The most frequent heatwave is based on the daily mean 90th temperature percentile and two days minimum duration. The least frequent heatwave is based on HI ≥ 90 lasting for a minimum of three days. The latter heatwave, is the definition in line with heatwave definition by MeteoSwiss, defined as "danger level 3" (MeteoSwiss, 2019).

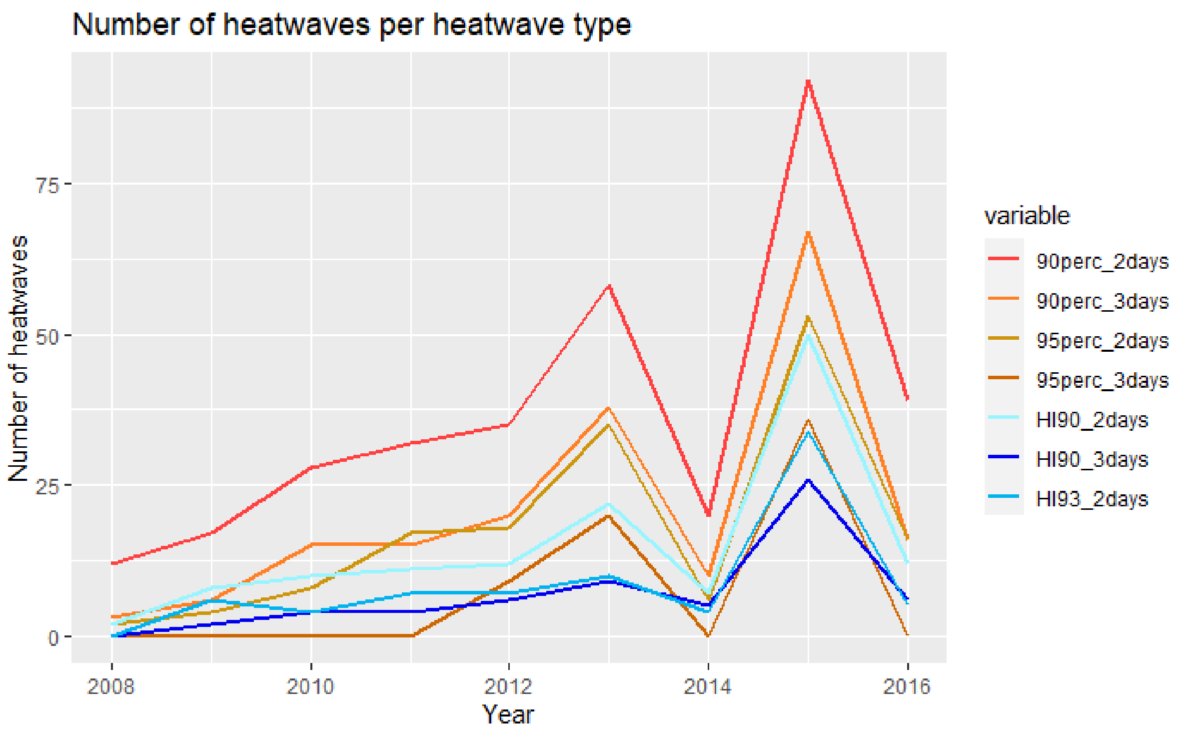

Figure 5. Number of heatwave events by different heatwave definitions. 90perc_2days and 90perc_3days: daily mean temperature above 90th percentile, lasting for minimum 2 and 3 days, respectively. 95perc_2days and 95perc_3days: daily mean temperatures above 95th temperature percentile, lasting for minimum 2 and 3 days, respectively. HI90_2days and HI90_3days: HI reaching 90 or higher for minimum 2 and 3 days in a row. 93perc_2days: HI reaching 93 or higher for minimum 2 days in a row. HI: Heat Index, based on daily maximum temperature and relative humidity.

4.1.2 Preterm birth

Table 6 represents the total number of PTB in Switzerland per canton and summer between 2008-2016. Data on PTB is missing for the cantons of *Neuchâtel* and *Geneva* in 2008, thus these two cantons were excluded from analysis for 2008. In total, the number of PTBs analysed in this study is 7,688. Over the nine years, there is a visible increase in the number of PTBs, which can be explained by the increase in total births (Figure 6).

Table 6. Total number of PTB cases per summer (June-August) and canton, between the years 2008-2016.

Preterm birth

Cantons	2008	2009	2010	2011	2012	2013	2014	2015	2016	Total	Mean
ZH+ZG+SH	175	155	173	163	200	173	173	199	207	1618	180
BE	91	86	74	92	101	101	108	86	101	840	93
LU	38	44	35	41	44	39	50	45	35	371	41
UR+OB+GL+GR	33	29	18	26	21	39	25	31	34	256	28
SZ+NW	20	15	13	16	18	21	15	19	16	153	17
FR	34	31	28	38	27	48	42	40	45	333	37
SO+JU	31	32	29	30	28	39	32	36	31	288	32
BS+BL	53	42	53	51	43	42	43	53	50	430	48
AR+AI+SG	69	76	56	55	64	47	63	46	56	532	59
AG	67	64	71	61	61	69	56	81	61	591	66
TG	23	22	33	25	23	22	19	31	30	228	25
TI	35	27	35	24	30	35	33	29	28	276	31
VD	63	99	90	76	117	77	101	87	79	789	88
VS	33	42	25	49	31	41	43	33	44	341	38
NE	0	15	20	26	19	26	30	19	19	174	19
GE	0	49	64	52	64	48	67	51	73	468	52
Total	765	828	817	825	891	867	900	886	909	7688	854
Mean	90	97	96	97	105	102	106	104	107	904	

Table 7 represents the PTB-rate in Switzerland per canton and summer between 2008-2016. Data on PTB is missing for *Neuchâtel* canton and *Geneva* canton in 2008, thus these two cantons were excluded from analysis for 2008. Overall, the PTB-rate remains stable and ranges from 41 to 45 PTBs per 1000 births across the summers in the nine year study period. When comparing cantons it is visible that *Schwyz + Nidwalden* has the lowest rate of 36 PTBs per 1000 births on average across the nine summers. *Neuchâtel* has the highest average rate of 51 PTBs per 1000 births across the eight summers.

Table 7. The mean summer PTB-rate per canton and summer (June to August). The rate is calculated by dividing PTBs/total births per day multiplied by 1000 and then calculating the daily mean rate per summer.

PTB / 1000 total births

Cantons	2008	2009	2010	2011	2012	2013	2014	2015	2016	Mean
ZH+ZG+SH	43.00	37.00	40.00	37.00	44.00	37.00	38.00	42.00	43.00	40.00
BE	41.00	35.00	34.00	37.00	41.00	41.00	45.00	35.00	39.00	39.00
LU	42.00	46.00	33.00	40.00	46.00	37.00	45.00	44.00	28.00	40.00
UR+OB+GL+GR	48.00	37.00	33.00	45.00	26.00	53.00	35.00	41.00	41.00	40.00
SZ+NW	43.00	41.00	36.00	29.00	33.00	41.00	28.00	39.00	34.00	36.00
FR	47.00	42.00	32.00	51.00	43.00	52.00	47.00	45.00	49.00	45.00
SO+JU	40.00	46.00	41.00	39.00	36.00	46.00	45.00	47.00	38.00	42.00
BS+BL	49.00	39.00	47.00	44.00	43.00	38.00	38.00	50.00	43.00	43.00
AR+AI+SG	50.00	53.00	40.00	39.00	46.00	35.00	44.00	28.00	35.00	41.00
AG	45.00	44.00	45.00	38.00	38.00	41.00	32.00	48.00	34.00	40.00
TG	35.00	46.00	56.00	45.00	38.00	35.00	26.00	42.00	40.00	40.00
TI	52.00	40.00	50.00	31.00	45.00	59.00	45.00	42.00	41.00	45.00
VD	35.00	48.00	46.00	39.00	59.00	38.00	49.00	42.00	36.00	44.00
VS	55.00	59.00	32.00	60.00	40.00	49.00	55.00	38.00	51.00	49.00
NE	NA	40.00	38.00	62.00	41.00	62.00	74.00	46.00	47.00	51.00
GE	NA	42.00	52.00	41.00	54.00	38.00	54.00	37.00	56.00	47.00
Mean	45.00	43.00	41.00	42.00	42.00	44.00	44.00	42.00	41.00	43.00

Figure 6 shows the temporal evolution of total births in Switzerland from January 2008 until December 2016. The black line in figure 6 represents the daily mean of births per month in Switzerland. There is a seasonal pattern, with fewer births in winter and two peaks in the summer/early autumn period. Moreover, the loess smoothing curve is included in red, which describes a clear upward long-term trend in the daily mean of births.

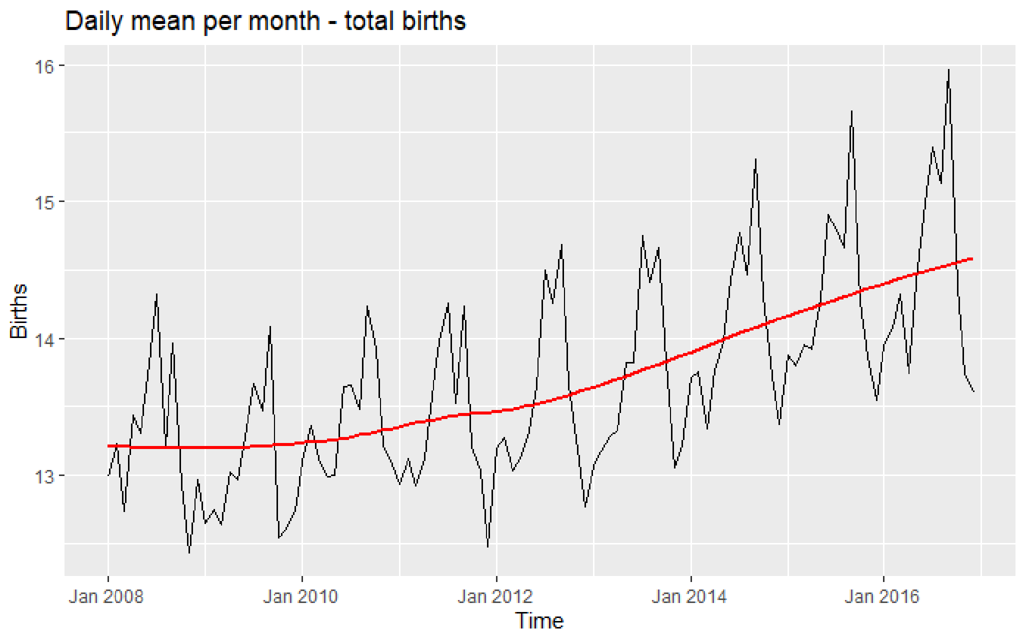

Figure 6. Temporal evolution of births in Switzerland. The black line shows daily mean per month from January 2008 until December 2016. The red line corresponds to the loess smoothing curve.

Figure 7 represents the daily mean of the number of PTB divided by the total number of singleton births, i.e. the PTB-rate, across the study period. According to the loess smoothing curve indicated in red, there is a negative trend happening throughout the timeline, with a slight increase in 2012.

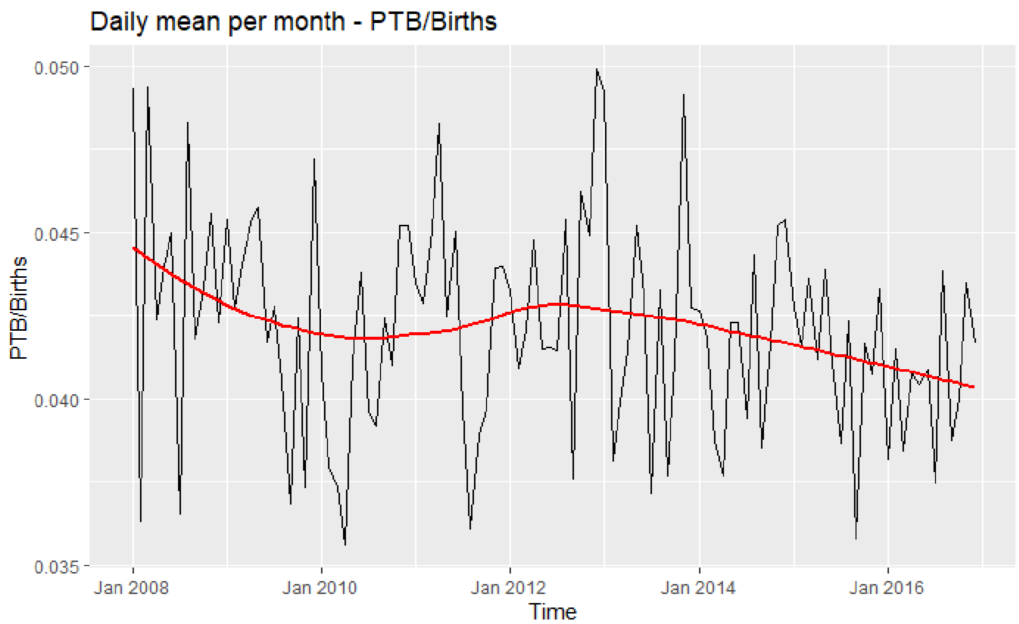

Figure 7. Temporal evolution of PTB/total births. The black line shows the daily mean in Switzerland from January 2008 until December2016. The red line corresponds to the loess smoothing curve.

The temporal evolution of the PTB/pregnancies-at-risk rate is shown in figure 8. The black graphs shows the daily mean value, from January 2008 until December 2016. The trend, which is represented in red, follows the PTB-rate in figure 7

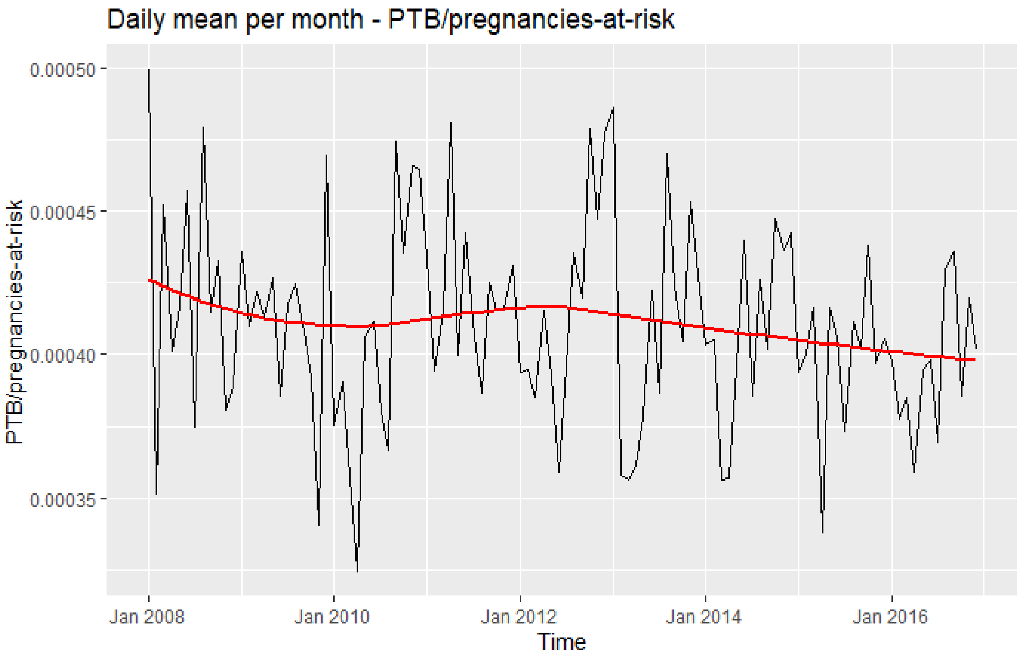

Figure 8. Temporal evolution of the PTB/pregnancies-at-risk rate. The black line shows the daily mean PTB/pregnancies-at-risk rate per month in Switzerland from January 2008 until December 2016. The red line corresponds to the loess smoothing curve.

Figure 9 represents for each year the temporal evolution of PTB per month (continuous line, left y-axis) as well as the temporal evolution of the PTB/pregnancies-at-risk rate (dashed line, right y-axis). By plotting the temporal evolution of the total number of PTBs in the same figure as the rate of PTB cases per total number of pregnancies at risk, it is possible to make a visual comparison between these two variables, as presented in figure 9 below. Principally, the total number of PTB-cases is on the left y-axis and the rate of PTBs per pregnancy at risk is on the right y-axis. Overall and as expected, there seems to be a positive relationship between the two variables.

In figure 9, there is a visible peak in total PTBs in August each year, which follows the seasonal pattern of total births seen in figure 6. However, there are conflicting results for some months where the total number of PTBs is relatively lower than in other years, while the PTB rate per pregnancies-at-risk is high. For example, in June and August 2008, the PTBs per pregnancies-at-risk-rate is higher than for the other years, although the total number of PTBs was lower in 2008 than in other summers.

Furthermore, it is also notable that in the summer of 2015 the most heatwaves were registered in Switzerland. Following the year 2015, it is also observable that 2013 was the second year with the most heatwaves in summer in this country. In figure 9, a high PTBs per pregnancies-at-risk-rate compared to other years was observed in August 2013.

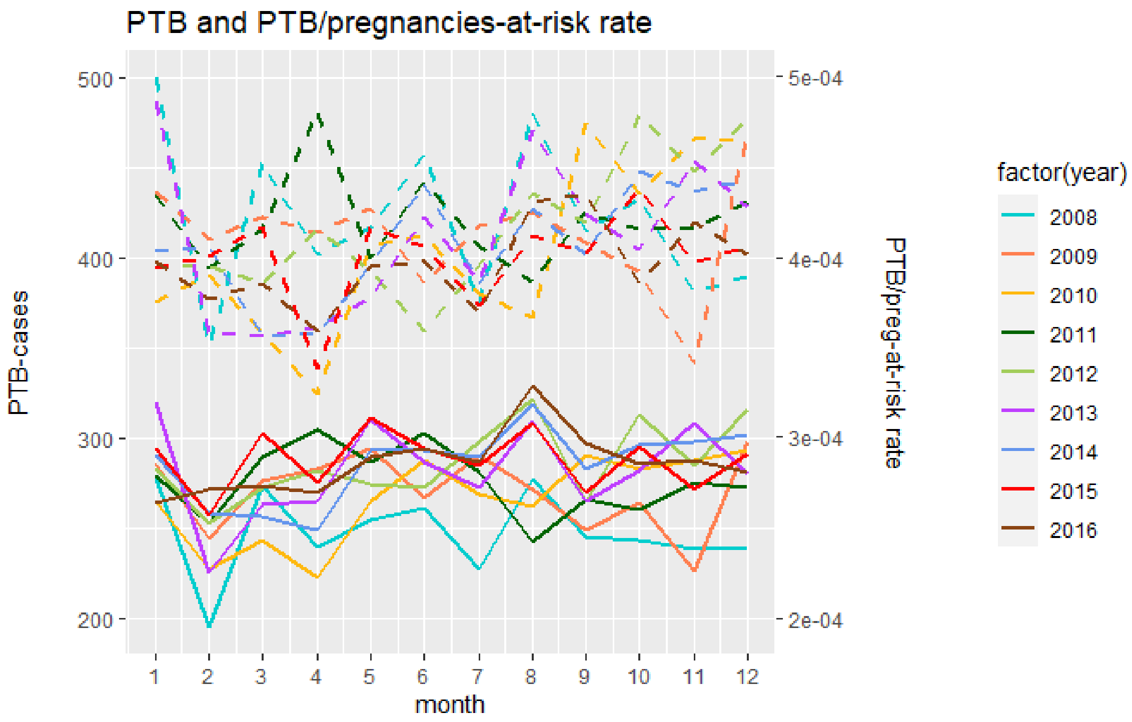

Figure 9. Comparison of the temporal evolution of preterm births in Switzerland (continuous line, left y-axis) and the PTB/pregnancies-at-risk rate (dashed line, right y-axis) between 2008-2016. The left y-axis represents the total number of PTB-cases in Switzerland per summer. The right y-axis represents the national mean rate per summer based on the total number of PTB-cases per day divided by the pregnancies at risk per day.

The temporal evolution of birth patterns was also done separately for mothers with Swiss citizenship/mothers with no Swiss citizenship, as well as for mothers above/below 31 years. As there was no clear difference between the four subgroups, these figures are found in the appendix (figure S6:S13)

4.2 Time-series analysis

A time-series analysis was done to evaluate the association between heatwave exposure the last day of pregnancy and PTB in each canton. The risk of having a PTB when exposed to a heatwave was measured in RR including a 95% confidence interval. This chapter shows the pooled results on RR from all cantons. The results are shown for the total population as well as for sub-categories in Table 8 below.

The main findings suggest that the RR ranges from 0.94 to 1.11 (CI: 0.78-1.13 and 0.91-1.36) in the total population depending on the heatwave. In Table 8 it is visible that the RR increases more for younger mothers with RR from 1.02 up to 1.35 (CI: 0.76-1.36 and 1.03-1.77) than for mother above 31 years with RR from 0.96 up to 1.06 (CI: 0.76-1.22 and CI: 0.82-1.36). For mothers without Swiss nationality the RR increased between 1.06 up to 1.52 (CI: 0.89-1.26 and CI: 1.16-2.00) which was higher compared to Swiss mothers with RR from 0.80 up to 1.06 (CI: 0.62-1.03 and CI: 0.90-1.24). Notably, a significant association was observed for mothers below 31 years using heatwave definition HI ≥ 93 for two days duration with RR: 1.35 (CI:1.03-1.77). Significant association was also observed for mothers with foreign citizenship when using both types of heatwave definitions, with RR: 1.27 (CI: 1.03-1.56) for heatwave definition daily mean temperature ≥ 95 percentile for two days, with RR: 1.29 (CI: 1.02-1.63) for heatwave definition HI ≥ 90 for two days and with RR: 1.52 (CI: 1.16-2.00) for HI ≥ 93 for two days.

Moreover, Table 8 shows that when defining a heatwave by daily mean temperature percentiles, the RR is higher when the temperature exceeded the 95th temperature percentile for two days rather than for a lower percentile for three days, similarly with what was observed for the second definition of heatwave based on HI. According to the results in Table 8, there is a clearer pattern of increased RR for the heatwave definitions based on daily mean temperature percentiles and a more inconsistent association between PTB and heatwave defined by HI. The results per canton on RR for each subcategory of mothers can be seen in the appendix (Table S1).

Table 8. The relative risk (RR) for having a preterm birth (PTB) when exposed to a heatwave the last day of pregnancy compared to when not being exposed to a heatwave. These results are the pooled RRs from all the cantons. The RR is shown for heatwaves by seven different definitions, for the total population as well as for sub-categories of mothers. Significant associations are marked with an asterisk.

Summarized RR for all cantons by all heatwave definitions

	90th perc. 2 days		95th perc. 2 days		90th perc. 3 days		95th perc. 3 days		HI ≥ 90, 2 days		HI ≥ 93, 2 days		HI ≥ 90, 3 days	
Population	**RR**	**2.5%-97.5%**	**RR**	**2.5%-97.5%**	**RR**	**2.5%-97.5%**	**RR**	**2.5%-97.5%**	**RR**	**2.5%-97.5%**	**RR**	**2.5%-97.5%**	**RR**	**2.5%-97.5%**
Total	1.06	[0.96-1.17]	1.07	[0.92-1.25]	1.02	[0.9-1.16]	1.08	[0.87-1.34]	1.02	[0.89-1.18]	1.11	[0.91-1.36]	0.94	[0.78-1.13]
Mother Above 31	1.04	[0.93-1.17]	1.06	[0.88-1.28]	0.98	[0.85-1.12]	1.06	[0.82-1.36]	0.96	[0.78-1.18]	1.02	[0.81-1.3]	0.96	[0.76-1.22]
Mother below 31	1.11	[0.97-1.27]	1.18	[0.97-1.44]	1.11	[0.94-1.3]	1.21	[0.94-1.56]	1.15	[0.93-1.41]	1.35	[1.03-1.77]*	1.02	[0.76-1.36]
Mother Swiss	1.06	[0.9-1.24]	1	[0.81-1.25]	1.03	[0.85-1.25]	1.01	[0.75-1.35]	0.89	[0.74-1.08]	0.94	[0.7-1.26]	0.8	[0.62-1.03]
Mother not Swiss	1.13	[0.98-1.3]	1.27	[1.03-1.56]*	1.06	[0.89-1.26]	1.28	[0.99-1.65]	1.29	[1.02-1.63]*	1.52	[1.16-2.00]*	1.28	[0.96-1.73]

* Significant association

Table 9 shows the RR (with 95% confidence intervals) of having a PTB associated with the type of heatwave based on daily mean temperature percentiles per canton. This first type of heatwave included only one variable, daily mean temperature. The thresholds for the first heatwave were defined at daily mean temperatures reaching the 90th and 95th percentile for a minimum of two and three days in duration.

According to the main results of table 9, statistically significant association between heatwave exposure and PTB is found in *Fribourg* and *Schwyz + Nidwalden* for specific heatwave definitions by mean temperature percentiles. In *Fribourg*, the association is found when the daily mean temperature equals the 90th percentile or higher for two and three days minimum (RR: 1.43, CI:1.02-2.02 and RR: 1.69, CI: 1.08-2.42, respectively), and when it equals the 95th percentile for two days minimum (RR: 1.98, CI:1.21-2.96). In *Schwyz + Nidwalden*, the association was observed when the daily mean temperature equals the 95th percentile or higher for three days minimum (RR: 2.35, CI: 1.09-5.08). In other cantons, the RR varied for each heatwave definition, showing both negative influence as well as a positive association with wide confidence intervals. The 95% confidence interval show the risk-ratio for each heatwave definition.

Table 9. The relative risk (RR) and risk-ratio when exposed to different heatwaves based on different daily mean temperature percentile thresholds. The heatwaves are defined by daily mean temperatures above 90th and 95th percentile, lasting for two or three days minimum. Significant associations are marked with an asterisk.

Relative risk per canton when exposed to heatwaves based on temperature percentiles

Heatwave:	**90th percentile, 2 days**		**95th percentile, 2 days**		**90th percentile, 3 days**		**95th perncentile, 3 days**	
Canton	**RR**	**2.5%-97.5%**	**RR**	**2.5%-97.5%**	**RR**	**2.5%-97.5%**	**RR**	**2.5%-97.5%**
ZH+ZG+SH	1.16	[0.96 - 1.4]	1.06	[0.8 - 1.41]	0.97	[0.76 - 1.23]	1.05	[0.75 - 1.47]
BE	0.87	[0.66 - 1.13]	0.83	[0.55 - 1.23]	0.84	[0.62 - 1.14]	0.61	[0.36 - 1.05]
LU	0.67	[0.43 - 1.04]	0.58	[0.26 - 1.29]	0.67	[0.4 - 1.11]	0.27	[0.06 - 1.12]
UR+OB+GL+GR	1.33	[0.86 - 2.05]	1.21	[0.65 - 2.25]	1.49	[0.92 - 2.43]	1.47	[0.76 - 2.81]
SZ+NW	1.37	[0.8 - 2.36]	1.78	[0.93 - 3.42]	1.37	[0.69 - 2.7]	2.35	[1.09 - 5.08]*
FR	1.43	[1.02 - 2.02]*	1.89	[1.21 - 2.96]*	1.61	[1.08 - 2.42]*	1.41	[0.75 - 2.63]
SO+JU	1.25	[0.82 - 1.91]	1.4	[0.74 - 2.64]	1.41	[0.85 - 2.36]	1.77	[0.84 - 3.74]
BS+BL	0.87	[0.6 - 1.26]	0.76	[0.42 - 1.36]	0.75	[0.47 - 1.22]	0.49	[0.18 - 1.32]
AR+AI+SG	0.96	[0.67 - 1.38]	1.18	[0.72 - 1.95]	1.07	[0.69 - 1.67]	1.58	[0.84 - 2.98]
AG	1.31	[0.97 - 1.77]	0.92	[0.56 - 1.51]	1.18	[0.82 - 1.7]	0.79	[0.43 - 1.48]
TG	1.16	[0.72 - 1.86]	1.36	[0.72 - 2.55]	1.38	[0.8 - 2.39]	1.36	[0.55 - 3.36]
TI	0.97	[0.59 - 1.61]	0.78	[0.38 - 1.6]	0.67	[0.37 - 1.23]	0.6	[0.25 - 1.44]
VD	0.9	[0.68 - 1.19]	0.81	[0.52 - 1.25]	1.01	[0.72 - 1.41]	0.9	[0.53 - 1.54]
VS	1	[0.68 - 1.46]	1.24	[0.73 - 2.12]	0.77	[0.47 - 1.27]	1.24	[0.65 - 2.39]
NE	0.85	[0.44 - 1.64]	0.55	[0.19 - 1.61]	0.94	[0.43 - 2.04]	0.45	[0.1 - 2]
GE	1.05	[0.74 - 1.49]	1.22	[0.7 - 2.11]	0.95	[0.63 - 1.43]	1.76	[0.88 - 3.52]

* Significant association

Table 10 shows the RR (with 95% confidence intervals) of having a PTB associated with the type of heatwave based on HI. The heatwaves are defined by HI thresholds 90 ≥ for two and three days, as well as HI ≥ 93 for two days. As seen in Table 5, the heatwave defined by HI never occurred in the *Schwyz + Nidwalden* cantons and only once for the mildest heatwave definition in the *Appenzell Ausserhoden*

+ *Appenzell Innerhoden + St Gallen* cantons That explains the null results obtained for this type of heatwave for these two cantons in Table 10. Table 10 shows that statistically significant association between this definition of heatwave exposure and PTB is found in *Fribourg* and *Thurgau* for specific heatwave definitions. In *Fribourg*, the association is found when the HI ≥ 90 for three consecutive days (RR: 2.62, CI: 1.09-6.33). In *Thurgau*, significant association is found when the HI ≥ 93 for two consecutive days (RR:2.84, CI: 1.04-7.74) and when the HI ≥ 93 for three consecutive days (RR: 2.75, CI:1.04-7.28). The 95% confidence interval show the risk-ratio for each heatwave definition.

Table 10. Relative risk (RR) when exposed to heatwaves based on different Heat Index (HI) and duration. The HI is based on daily maximum temperature and relative humidity. The heatwaves are defined by HI thresholds 90 ≥ for two and three days, as well as HI ≥ 93 for two days Significant associations are marked with an asterisk.

Relative risk per canton when exposed to heatwaves based on heat index

Heatwave:	**HI ≥ 90, 2 days**		**HI ≥ 93, 2 days**		**HI ≥ 90, 3 days**	
Canton	**RR**	**2.5%-97.5%**	**RR**	**2.5%-97.5%**	**RR**	**2.5%-97.5%**
ZH+ZG+SH	1.22	[0.95 - 1.57]	0.99	[0.65 - 1.5]	1.04	[0.71 - 1.52]
BE	0.87	[0.53 - 1.42]	0.59	[0.18 - 1.92]	0.76	[0.41 - 1.43]
LU	0.72	[0.36 - 1.47]	0.53	[0.19 - 1.48]	0.66	[0.2 - 2.16]
UR+OB+GL+GR						
SZ+NW	1	[1 - 1]	1	[1 - 1]	1	[1 - 1]
FR	1.86	[0.93 - 3.73]	1.07	[0.24 - 4.74]	2.62	[1.09 - 6.33]*
SO+JU						
BS+BL	0.84	[0.56 - 1.27]	0.7	[0.39 - 1.25]	0.78	[0.46 - 1.32]
AR+AI+SG	0	[0 - 2.74e+78]	1	[1 - 1]	1	[1 - 1]
AG						
TG	1.66	[0.66 - 4.15]	2.84	[1.04 - 7.74]*	2.75	[1.04 - 7.28]*
TI	0.59	[0.27 - 1.31]	0.59	[0.26 - 1.31]	0.45	[0.06 - 3.07]
VD	0.95	[0.55 - 1.64]	1.15	[0.59 - 2.23]	0.86	[0.4 - 1.83]
VS	1.05	[0.76 - 1.46]	1.09	[0.76 - 1.55]	1.28	[0.88 - 1.87]
NE	0.43	[0.09 - 2.06]	0.34	[0.04 - 2.9]	0.39	[0.04 - 3.35]
GE	0.95	[0.68 - 1.34]	0.9	[0.59 - 1.36]	1.33	[0.89 - 2.01]

*Significant association

The results per canton on RR for the sub-categories dividing mothers into Swiss citizen/not Swiss citizen and above/below 31 years of age are shown in the appendix in tables (S2 and S3). A sensitivity analysis was done to validate the results in the time-series analysis. This sensitivity analysis included a three-day exposure-response lag, studying whether heatwave exposure might induce PTB up to three days after exposure. This analysis summarized the results from all cantons, showing the RR of heatwave exposure and PTB on a national level. Total population as well as population sub-groups were included in analysis. The results are shown in appendix (Table S1). The results from the sensitivity analysis shows a lower association but highly unprecise between heatwave exposure and PTB than the analysis without lag (Table 8).

5. Discussion

This master thesis assessed heatwaves and PTB in Switzerland. Furthermore, the aim was to investigate any plausible relationships between the two variables. This chapter discusses the results of the descriptive and time-series analyses. The purpose here is to answer the research question on whether there is an increased risk of having PTB during heatwaves in Switzerland. As a secondary aim, to evaluate if there is a different effect using diverse definitions for the heatwave phenomena and whether particular groups of women are at greater risk. Moreover, this chapter looks at strengths and weaknesses in this study, and discusses limitations and possible confounding factors. Finally, future recommendations about this topic will be exposed.

5.1 Overview: Heatwaves and PTB in Switzerland

Two different types of heatwaves based on different variables were considered in this study, because there exists no formal definitions of heatwave. One heatwave definition is based on daily mean temperature percentiles. The daily mean temperature includes night temperature, which means that the average temperature throughout day and night was very warm (above the 90^{th} and 95^{th} percentile). The objective of using this definition was to capture an event with high temperature, which lasts for a longer duration. The duration threshold for this heatwave definition was set to a minimum of two and three days. The thresholds for the type of heatwave based on daily mean temperature were chosen based on current heatwave definitions at MeteoSwiss (MeteoSwiss, 2021). Using a minimum duration of four days was not attempted, as only a few such heatwave events appeared to have occurred in Switzerland during 2008-2016. That is not favourable for the time-series analysis. The second heatwave definition is based on apparent temperature using HI, which includes both relative humidity and maximum temperature parameters. When studying adverse health effects by high temperature exposure, it is important to also consider the compound effect of temperature and relative humidity (Mukherjee et al., 2021). Studies show that the combination of air temperature and relative humidity has a cumulative effect, decreasing the body's ability to cool down and adds to heat stress (Buzan & Huber, 2020). The thresholds for the type of heatwave based on HI were chosen based on previously used heatwave definitions at MeteoSwiss (MeteoSwiss, 2019).

This study describes the temporal evolution of the heatwaves used in this study, based on the weather data from MeteoSwiss. The occurrences varied for the two different heatwave types defined in this study. The type of heatwaves defined by daily mean temperature percentiles occurred more frequently in all cantons from 2008-2016, compared to the heatwaves defined by HI (Tables 4 and 5). This difference indicates that this study uses two heatwave definitions which are different from each other, not only in terms of parameters, but also in terms of frequency.

When using temperature percentiles and cantons for the analysis, the actual air temperature threshold identifying a heatwave will vary between cantons. Because the climate varies in Switzerland, temperatures at the 90^{th} percentile in Aargau are expected to differ from the 90^{th} temperature percentile in Ticino. This method considers that the people living in different cantons are adapted to different summer temperatures. Defining heatwaves by cut-off temperature percentiles and for a varying duration of days have been done in many similar studies before (Wang et al., 2013; Diouf et al., 2021; Ilango et al., 2020). On the contrary, the second heatwave definition based on HI which is more in line with the definition by MeteoSwiss (MeteoSwiss, 2019), does not account for human adaptation to different temperatures in different parts of Switzerland.

This study aimed to assess the temporal evolution of births and PTBs in Switzerland over the chosen study period. Table 6 shows an increase in the total number of PTBs. The PTB increase seen in Table 6, matches the increase in total births seen in Figure 6. However, despite the increasing PTB cases, there is a visible decrease in the PTB/total births ratio as well as the PTB/pregnancies-at-risk ratio in the nine year study period, as shown in Figures 7 and 8, respectively. Figures 8 and 9 both show a spike in PTB/births and PTB/pregnancies-at-risk in 2012. Due to time constraints, what caused this spike was not investigated in the work of this thesis, but it would be interesting to look into this in more detail in the future.

The results in this study show a clear seasonal pattern with increased births in the late summer period and a significant drop in births in the winter period (Figure 6). This is in line with other research findings, which highlight the importance to control for seasonal conception when studying PTB in association with environmental variables (Weinberg et al., 2015).

5.2 Association between heatwaves and PTB

The main objective of this study was to determine whether there is an increased risk of having a PTB when exposed to heatwaves in Switzerland. With these two different types of heatwave definitions and combination of thresholds, for the first time in this country the effects of using different heatwave definitions were analysed to obtain more comprehensive results. Moreover, the study aimed to assess whether the type of heatwave definition effect the results, and additionally, whether there is a difference in risk depending on age and nationality of the mother.

To describe the results on PTB and heatwave exposure in more detail, Table 8 shows the results for the pooled RR. According to Table 8, although the results are unprecise, there is an increased risk in having a PTB when exposed to a heatwave for the total population as well as for all subcategories of mothers nationwide. Moreover, the RR is higher for heatwaves defined by higher temperature thresholds for a shorter duration, compared to using lower temperature thresholds lasting for a longer duration. On the other hand, there is more homogeneity in the RR when defining a heatwave by daily mean temperature in comparison to the heatwaves defined by HI, which shows a more inconsistent pattern in RR. This is an interesting finding, as MeteoSwiss changed their own heatwave definition from being based on HI to instead use a daily mean temperature variable. Their reasoning is, that daily mean temperature is a more robust variable than HI (MeteoSwiss, 2021b), and that is interesting statement to consider when comparing the results for the different heatwave definitions in Table 8. Notably, although cantons *Basel Stadt + Basel Landschaft, Geneva* and *Valais* had most heatwave events based on HI (Table 5), no significant association was observed there.

Another objective of this study was to measure potential differences in risk depending on age and nationality of the mother. The results in Table 8 show a higher RR for mothers younger than 31 years compared to older mothers, as well as for mothers with foreign citizenship compared to Swiss mothers. These findings are in line with similar studies finding a higher risk among younger mothers (Basu et al., 2010), and potentially to other results finding differences in risk when comparing ethnicities (Basu et al., 2010; Goldenberg et al., 2018; Räisänen et al., 2013).

However, when reading Tables 9 and 10 the results on RR are inconsistent showing no clear pattern when conducting analysis on cantonal level. This study found statistically significant association on specific cantons between heatwave exposure and PTB. In particular, significant association was observed in *Fribourg*, *Schwyz + Nidwalden* and *Thurgau* for specific heatwave definitions. The reason might be that there are too few PTB cases in many cantons to perform a reliable statistical analysis. Other researchers have also studied PTB in relation to high temperatures in temperate climate, and found weak associations or none (Wolf & Armstrong, 2012; Auger et al., 2014). For example, a study done in Canada analysing birth data between 1982-2010 and exposure to temperatures above 32°C for consecutive days for 19,829 births, and found no association between the factors for preterm delivery (Auger et al., 2014). Another study by Wolf and Armstrong (2012), looked at low birth weight and PTB in association with high temperatures in Germany. That study showed only weak and inconsistent associations between the factors, with no clear evidence to support the hypothesis that there is a clear and strong association. Nevertheless, numerous studies show that extremely high temperatures and heatwaves can have adverse effects on birth outcomes (Vicedo-Cabrera et al., 2014; Basu et al., 2010; Zhang et al., 2017).

We should acknowledge several factors that can affect the estimates of the analysis. Heatwave classifications, accurate exposure estimates, accurate gestational ages and the methods used are all crucial to this kind of research (Zhang et al., 2017, Wolf & Armstrong., 2012). An alternative approach to the one used in this study would be to use larger regions for analysis, i.e. to merge more cantons together. This would mean more births are included in each time-series analysis which could impact the statistical analysis, although more exposure estimates would increase in misclassification with larger areas. As a recommendation for future research, it would be interesting to follow up on this approach.

It could be, that the resolution of this temperature data is too large to estimate temperature exposure, as well as that some cantons are too large to be given one single value for daily temperatures. Such wide ranges may not yield accurate estimates on the temperatures that each pregnant woman experienced in Switzerland. There were 710,360 births in total in Switzerland from 2008 to 2016, and 29,831 were classified as PTBs (4.2% of the total). Having accurate data on so many pregnancies is a challenge. Other studies analysing heatwaves or extreme heat exposure and PTB have used other exposure classification methods. Basu et al. (2010), as well as Ilango et al. (2020), identify exposure by residential zip code and temperature data from weather stations based on proximity. Such exposure classification might be more precise, and show a more realistic maternal temperature exposure.

Other studies find clearer relationships between heatwave exposure and PTBs (Zhang et al., 2017), and as heatwaves are expected to increase (Dosio et al., 2018), it might be a growing issue in Switzerland. This means, although this study could not prove consistent association between heatwaves (as defined in this study) and PTB in Switzerland, more research is needed. Climate projections are projecting an increase in heatwave magnitude and frequency in Switzerland (CH2018, 2018). This could mean that the association between heatwaves and PTB found in warmer climates (Carolan-Olah et al., 2013; Zhang et al., 2017), is also probable in Switzerland with climate change.

The results from the sensitivity analysis which included a three-day exposure lag response are shown in Table S1 in appendix. When comparing the result in Table S1, the RR is constantly lower for all population categories and heatwave definitions when compared to the RR without any lag (Table 8), with three exceptions only. Those were heatwaves defined by:90th temperature percentile for two days (mothers below 31 years), and HI ≥ 93 for two days and HI ≥ 90 for three days (foreign mothers). Moreover, when including a lag response in the model, the analysis becomes more complex. This in turn, is a limitation and is notable as the confidence intervals get larger. Besides, it is possible that when analysing a heatwave phenomenon which lasts for more than one day, it is more difficult to include a lag response as the exposure event itself is already extended over a longer period and varies in length.

5.3 Strenghts and limitations

This study used two different types of heatwave definitions, based on different variables. These different types of heatwaves were defined with four and three different combinations of temperature and duration thresholds respectively. This study takes into consideration, that temperature can be measured in different ways. In addition, the effect of heatwave exposure might increase with increasing duration of the heatwave. This is a central strength in this study. The analysis includes a pregnancies-at-risk-approach, and considers the change in gestational week each day. This is another distinctive strength in this study, because seasonal conception patterns and elevated PTB risk with gestational age are accounted for to minimize bias (Darrow et al., 2009; Vicedo-Cabrera et al., 2014).

Furthermore, an advantage in this study is that the average daily temperature data in this study comes from a gridded temperature data set. That data set was population-weighted before daily averages per canton were calculated. By using 2x2 km large grid cells offering high resolution temperature data, this method provides better average estimates on temperature than making an average across big regions. In addition, this study is done as a nationwide analysis, minimizing selection bias from the study sample.

A common limitation in many epidemiological studies are confounding factors. This is adjusted for by design in this study by using robust statistical models. The possible confounders are multifactorial and range from physical, social, biological and environmental (Räisänen et al., 2013). As the etiology of PTB is not fully understood and confounders are multifactorial (Räisänen et al., 2013), to have accurate data on the number of pregnancies used in this study is a challenge. On the other hand, although the long-term and seasonal trends were controlled in the models through a time-stratified approach, and these accounted for overdispersion, some limitations inherent in any ecological study should be considered such as the fact that the results cannot be extrapolated at an individual level. Furthermore, the data of daily climatic variables did not represent individual exposure (Barceló et al., 2016; Gelfand, 2000)

This study looked at different outcomes between mothers with Swiss citizenship and mothers with foreign citizenship, and at mothers above and below 31 years of age. When pooling the results from all cantons, there is a notable difference in risk between young and older mothers, as well as for Swiss and foreign mothers. This result was not found for these sub-categories when looking at cantonal level. The reason is likely to be that the number of PTBs is too low for a powerful statistical analysis on such small scale. However, there might not be a significant difference in socioeconomic structures or other influential factors between the different cantons in Switzerland as this kind of characteristics are more significant in low- and middle income countries (Basu et al., 2017). Other indicators might have shown a better segregation, such as behavioural habits (Basu et al., 2017; Räisänen et al., 2013).

As already discussed, the exposure classification could be a limitation in this study. Exposure is identified by cantonal residence, with an average temperature for whole cantons. Thus, the temperature resolution is rather large. Other studies have highlighted the importance of exposure classification for estimating associations between heatwaves and PTB (Wolf & Armstrong, 2012). The exposure classification is something worth developing in this study, however due to time restrictions it is outside the scope of this study.

Another limitation in this study is that the birth data includes both planned and unplanned Caesarion births. Ideally, planned Caesarion births would have been excluded, however the data on what Caesarions were planned or not was not available. The planned Caesarions are expected to be insignificant in this study, particularly as they are most of the time scheduled after 37 weeks of gestation (Hirslanden, 2021). Furthermore, this study consider the cause for unplanned Caesarions to be comparable to the cause for a PTB. Therefore, PTB by Caesarion and natural birth are considered equal and unplanned Caesarion births before 37 gestational weeks are treated just as the non-Caesarion PTB cases in this study.

When dividing mothers into categories may increase the confidence intervals, because we have split the data into smaller groups and loose statistical power. For this reason, this study did not divide PTB into sub-categories based gestational week, as it was considered that the data count for extremely preterm (<28 weeks) and very preterm (28-32 weeks) would be too low for statistical analysis. Therefore, one PTB category was used (<37 gestational weeks).

5.4 Future research

The aim of this master thesis was to offer a better overview over the situation on PTB and hot summers in Switzerland. It also aimed to highlight any possible association between heatwaves and early deliveries by mothers. The results in this study give a more comprehensive overview over the situation based on available birth data and the heatwave definitions used in this study. It has shown a seasonal birth pattern and temporal PTB-rates for the nine-year study period. However, more research is needed to better understand the association between PTB and heatwave exposure in Switzerland.

The exposure classification in this study is based on mean temperatures for whole cantons. It would be worth to develop the exposure classification in order to obtain more precise temperature exposure for each individual in future studies. Using individual data would maximise the use of available data in analyses and could generate more precise results. Moreover, to analyse the effect other environmental variables has on the association between heatwaves and PTB would be meaningful to better understand environmental hazards to pregnancies.

Furthermore, to study any influence socioeconomic variables have on association between heatwaves and PTB is important. This information is important in order to identify particular groups of women at risk and to improve existing public health policies and prevent further health burden in the future due to climate change.

Another possibility for advancing the analysis in this study is to merge more cantons creating larger regions as a next step in this research. In Table 6 it is shown that the total number of PTBs per summer is 854 on average in Switzerland between 2008-2016. This equals to 9.3 PTBs per day on average in each canton cluster used in this study. As the data was split into 16 canton clusters, the number of PTBs is very low. Splitting the data into larger regions would mean more births per region and more statistical power for statistical analysis. Due to time constraint, this was not done in this study.

To assess the future situation, climate change and current climate projections should be considered. This study suggests to adapt the exposure classification, and rather than creating averages for whole cantons, to try to minimize the resolution of the temperature data, with the aim to get more accurate exposure data. Besides, exploring other heatwave definitions with other thresholds would also be meaningful. For example, heatwaves lasting for a longer period of time would be interesting to analyse, and also lower temperature percentile thresholds or HI values. Another interesting heatwave definition to explore would be to use daily minimum temperature with different temperature percentile thresholds.

In another attempt to study possible association between PTB and heatwave exposure, focusing on maternal residence would be interesting in order to study whether there is an urban-heat-island effect and a higher risk of PTB when living in a city compared to a countryside surrounding. To the authors knowledge, this has only been done in one study before which accounted for the degree of urbanisation of maternal residence (Cox et al., 2016).

6. Conclusion

This thesis gives an overview on PTB and heatwaves in Switzerland between the years 2008 to 2016. To assess whether heatwave exposure increases the risk of PTB two different types of heatwaves were identified. They are based on prior and current heatwave definitions by MeteoSwiss. One type based on daily mean temperature percentiles, defined by temperatures exceeding the 90th and 95th percentile for a duration of two and three days each. The other type of heatwave was based on daily maximum temperature and mean relative humidity, i.e. HI. Three different combinations of thresholds are used: both the HI reaches 90 or higher for at least two and three days in a row, as well as HI reaches 93 for at least two days in a row.

Without considering a stratified analysis, the analysis reveal no association for the whole country, but for specific cantons: *Fribourg* (RR: 1.43, CI: 1.02-2.02; RR: 1.89, CI: 1.21-2.96; RR: 1.61, CI: 1.08-2.42, RR: 2.62, CI: 1.09-6.33), *Schwyz + Nidwalden* (RR: 2.35, CI: 1.09-5.08) and *Thurgau* (RR: 2.84, CI: 1.04-7.74; RR:2.75, CI: 1.04-7.28) for specific heatwave definitions. Yet there is a clear pattern showing a positive association when pooling the cantonal results. Moreover, the pooled results show a more consistent increase in RR when using heatwave definitions based on daily mean temperature compared to HI. For the total population, heatwaves based on daily mean temperature increased the risk of PTB by 2% to 8%, and heatwaves based on daily maximum temperature and mean relative humidity increased the risk by -6% to 11%. In the stratified analysis significant association was observed for mothers below 31 years (RR: 1.35, CI: 1.03-1.77) and for mothers with foreign citizenship (RR: 1.27, CI: 1.03-1.56; RR: 1.29, CI: 1.02-1.63 and RR: 1.52, CI: 1.16-2.00) for specific definitions.

The conclusions from the results are, first, an indication of a positive association between PTB risk and heatwaves was found, mainly in young and non-Swiss mothers, and for specific cantons. Second, the variables and the thresholds used for heatwave definitions affected the results. Finally, more research is needed to better understand the association between heatwave exposure and PTB in Switzerland.

Appendix

The appendix comprises the following items:

- Figures S1-S2: Temporal evolution of PTB for foreign and Swiss mothers
- Figures S3-S4: Temporal evolution on PTB/pregnancies-at-risk for foreign and Swiss mothers
- Figures S5-S6: Temporal evolution of PTB for mothers below and above 31 years
- Figures S7-S8: Temporal evolution on PTB/pregnancies-at-risk for mothers below and above 31 years
- Table S1: Sensitivity analysis: Table with the summarized RR from all cantons including a three-day response lag for all seven heatwave definitions and population categories
- Table S2:The RR per canton for all heatwave definitions for Swiss and foreign mothers
- Table S3: The RR per canton for all heatwave definitions for mothers below and above 31 years

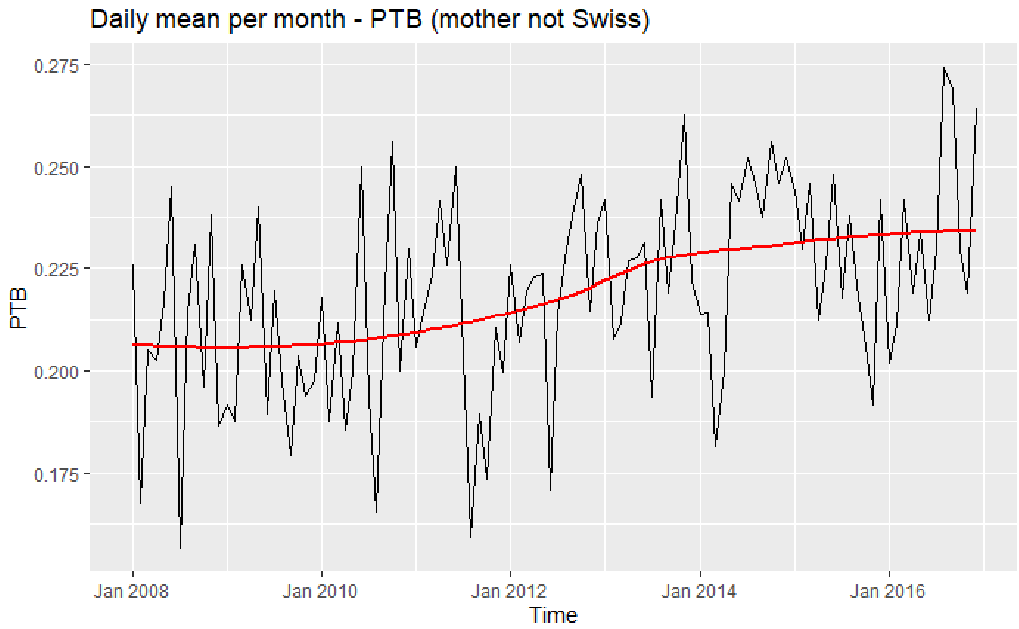

Figure S 1: Temporal evolution of PTB for mothers with no Swiss citizenship. The black line represents daily mean value per month. The red line corresponds to the loess smoothing curve. Starting in January 2008 and ending in December 2016.

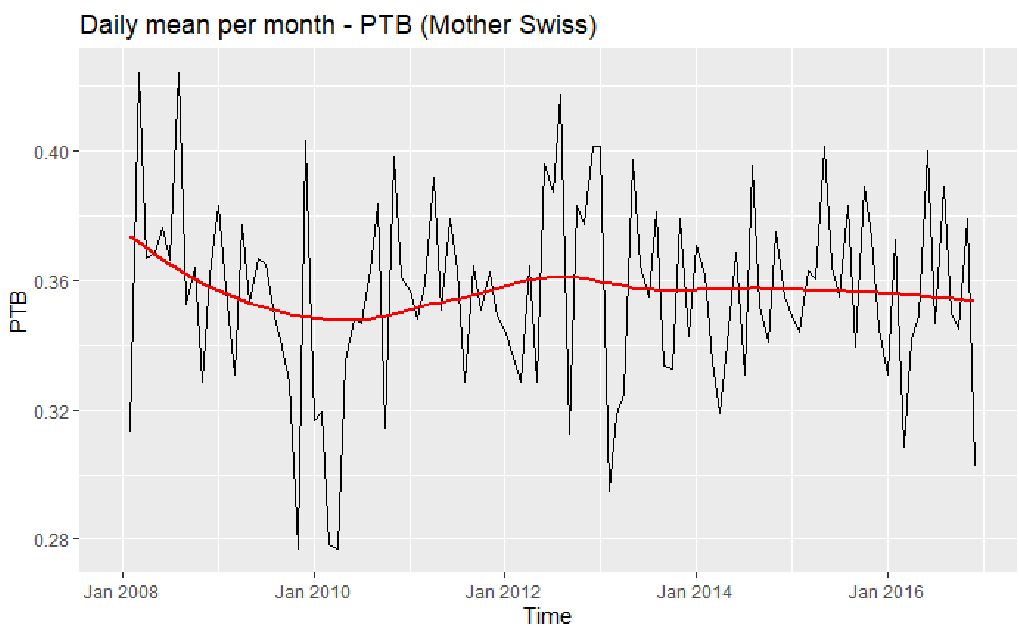

Figure S 2: Temporal evolution of PTB for mothers with Swiss citizenship. The black line represents the daily mean per month. The red line corresponds to the loess smoothing curve. Starting in January 2008 and ending in December 2016.

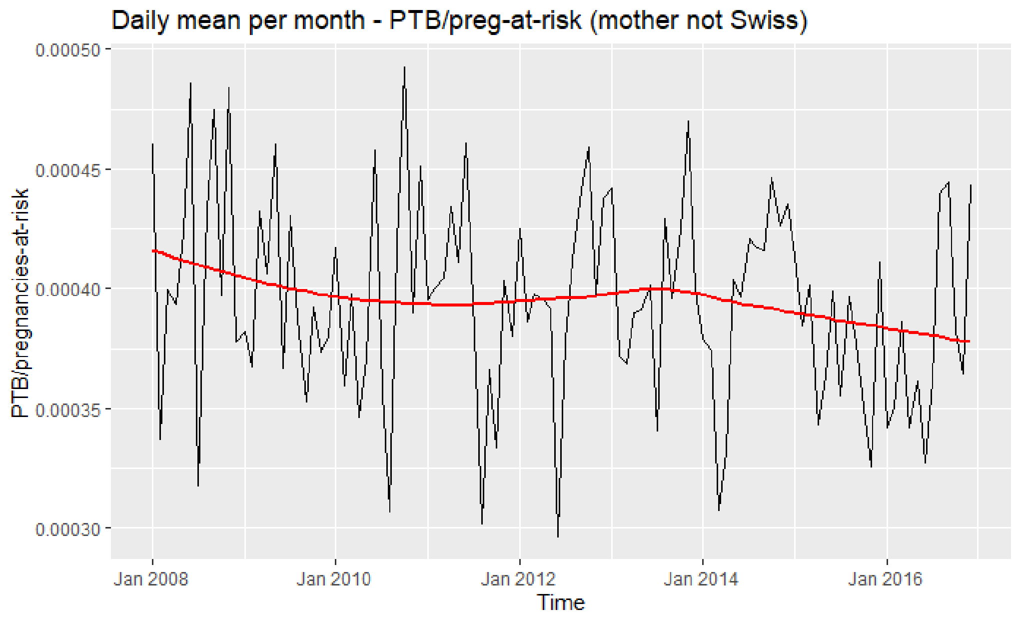

Figure S 3. Temporal evolution of PTB/pregnancies-at-risk for mothers with no Swiss citizenship. The black line represents the daily mean per month. The red line corresponds to the loess smoothing curve. Starting in January 2008 and ending in December 2016..

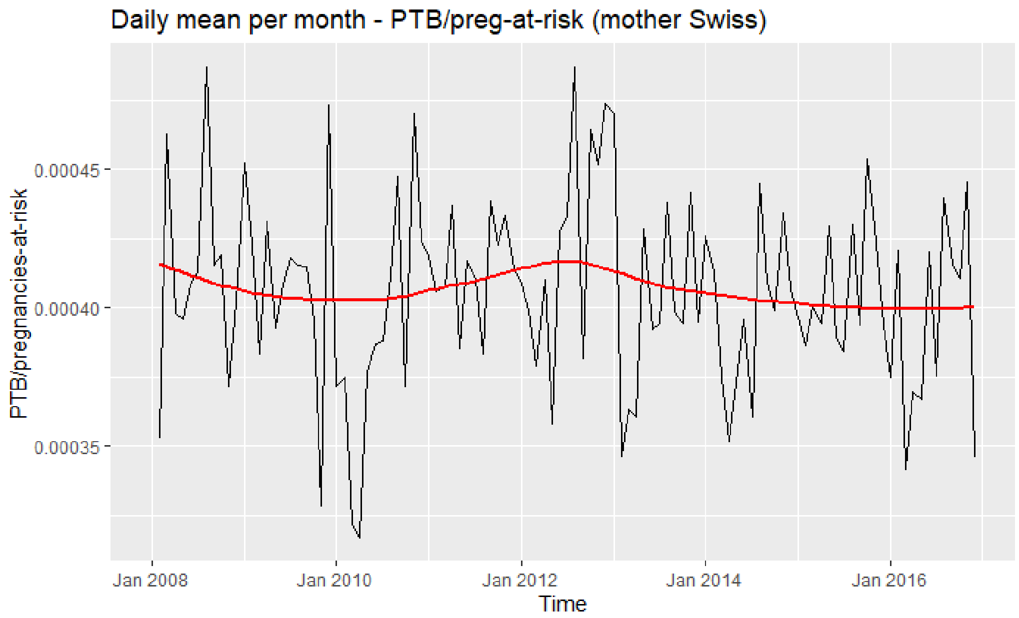

Figure S 4. Temporal evolution of PTB/pregnancies-at-risk for mothers with Swiss citizenship. The black line represents the daily mean per month. The red line corresponds to the loess smoothing curve. Starting in January 2008 and ending in December 2016.

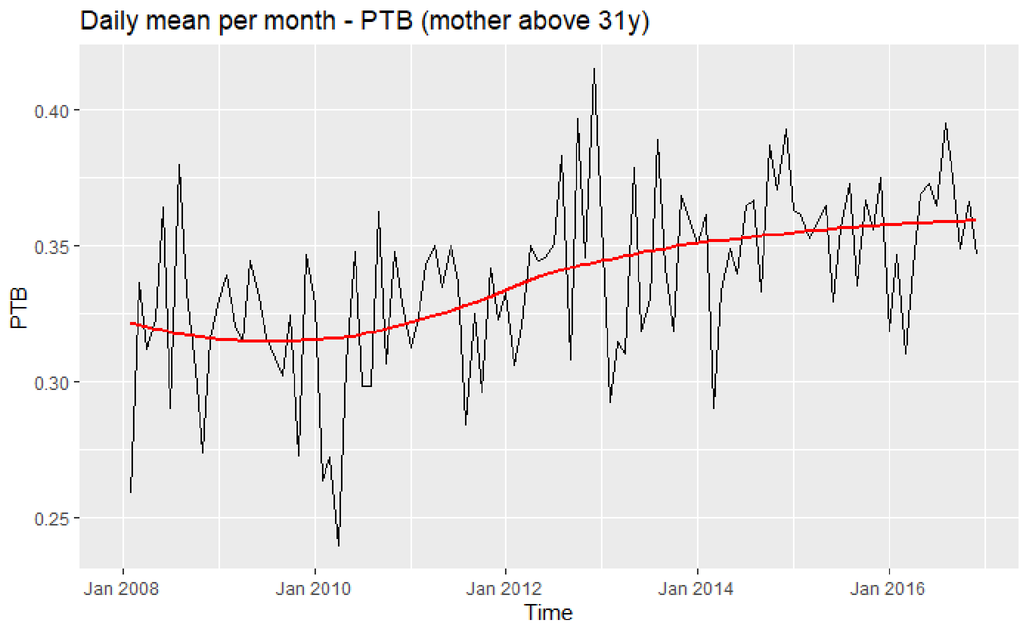

Figure S 5. Temporal evolution of PTB for mothers above 31 years old. The black line represents the daily mean per month. The red line corresponds to the loess smoothing curve. Starting in January 2008 and ending in December 2016.

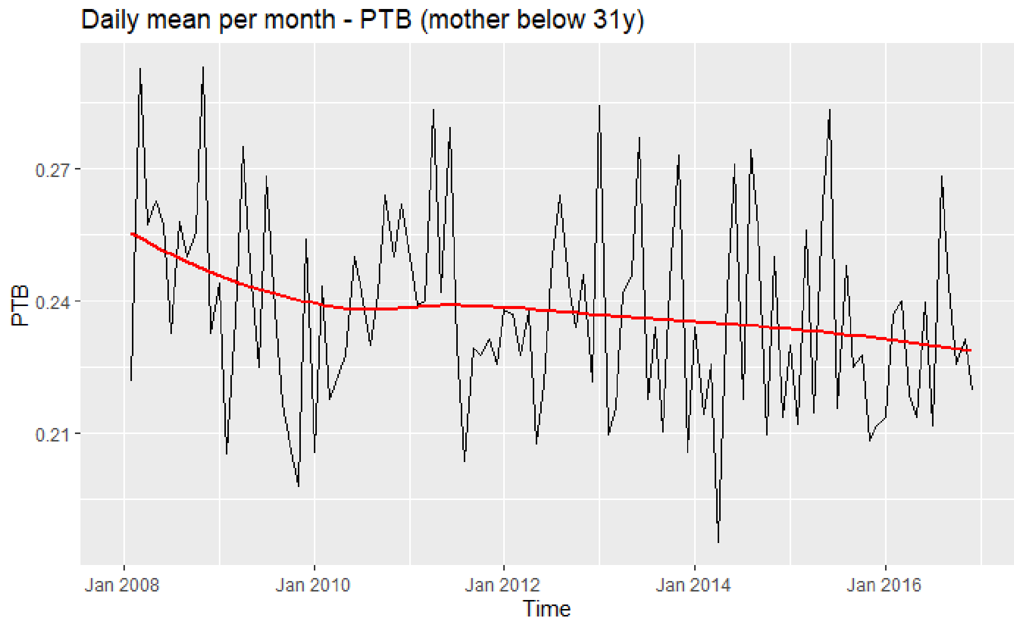

Figure S 6: Temporal evolution of PTB for mothers below 31 years old. The black line represents the daily mean per month. The red line corresponds to the loess smoothing curve. Starting in January 2008 and ending in December 2016.

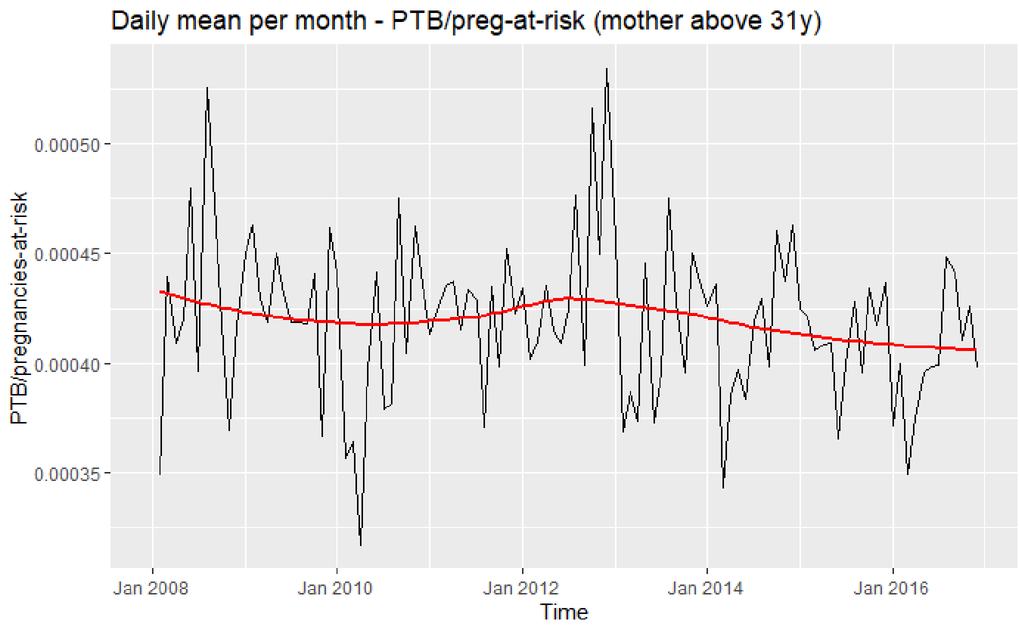

Figure S 7. Temporal evolution of PTB/pregnancies-at-risk for mothers above 31 years old. The black line represents the daily mean per month. The red line corresponds to the loess smoothing curve. Starting in January 2008 and ending in December 2016.

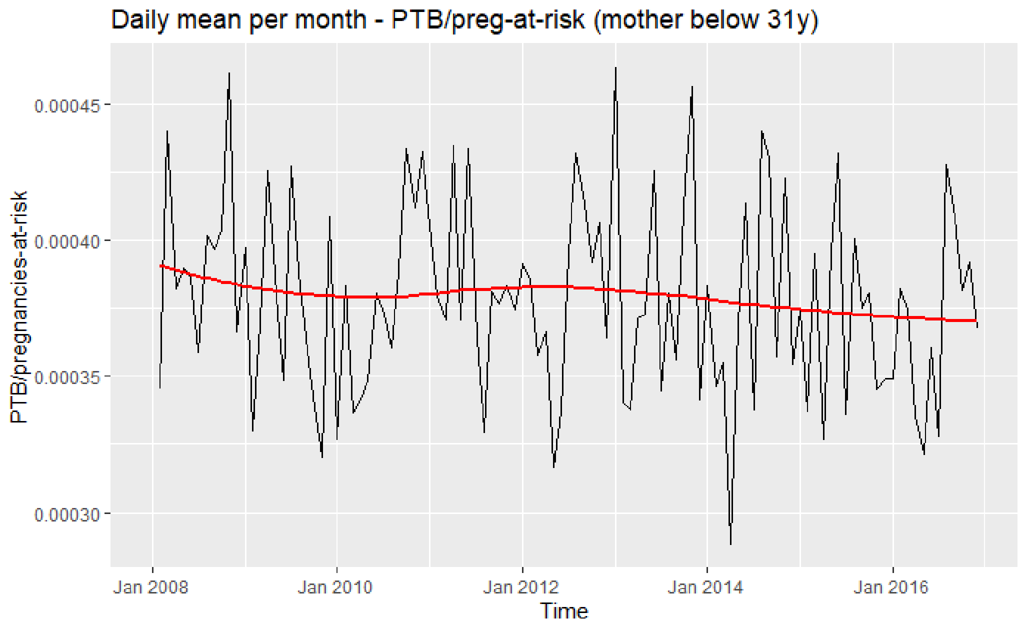

Figure S 8. Temporal evolution of PTB/pregnancies-at-risk for mothers below 31 years old. The black line represents the daily mean per month. The red line corresponds to the loess smoothing curve. Starting in January 2008 and ending in December 2016.

Summarized RR including 3 days lag for all cantons by all heatwave definitions

	90th perc. 2 days		95th perc. 2 days		90th perc. 3 days		95th perc. 3 days		HI ≥ 90, 2 days		HI ≥ 93, 2 days		HI ≥ 90, 3 days	
Population	**RR**	**2.5%-97.5%**	**RR**	**2.5%-97.5%**	**RR**	**2.5%-97.5%**	**RR**	**2.5%-97.5%**	**RR**	**2.5%-97.5%**	**RR**	**2.5%-97.5%**	**RR**	**2.5%-97.5%**
Total	1	[0.84-1.14]	0.9	[0.75-1.15]	0.9	[0.79-1.08]	0.9	[0.73-1.14]	0.9	[0.72-1.08]	1	[0.75-1.29]	0.8	[0.65-1.06]
Mother Above 31	0.9	[0.74-1.05]	0.8	[0.65-1.1]	0.8	[0.7-1.01]	0.9	[0.63-1.13]	0.8	[0.61-1.15]	0.9	[0.66-1.34]	0.8	[0.6-1.12]
Mother below 31	1.2	[0.92-1.45]	1.1	[0.85-1.54]	1.1	[0.86-1.32]	1.1	[0.77-1.57]	0.9	[0.68-1.3]	1.2	[0.79-1.83]	1	[0.65-1.4]
Mother Swiss	0.9	[0.77-1.16]	0.9	[0.66-1.11]	0.9	[0.71-1.15]	0.9	[0.66-1.18]	0.7	[0.51-0.91]	0.7	[0.48-1.04]	0.7	[0.48-0.93]
Mother not Swiss	1.1	[0.87-1.29]	1.2	[0.91-1.69]	1	[0.78-1.24]	1.1	[0.76-1.57]	1.3	[0.92-1.72]	1.6	[1.05-2.35]*	1.2	[0.85-1.79]

* Significant association

Table S 1. Sensitivity analysis: the relative risk (RR) for having a preterm birth (PTB) when exposed to a heatwave (in June, July and August) up to three days before giving birth compared to when not being exposed to a heatwave. These results are the pooled RRs from all the cantons. The RR is shown for heatwaves by seven different definitions, for the total population as well as for sub-categories of mothers.

Population	Canton	90th percentile, 2 days	95th percentile, 2 days	90th percentile, 3 days	95th perncentile, 3 days	HI ≥ 90, 2 days	HI ≥ 93, 2 days	HI ≥ 90, 3 days
		RR 2.5%-97.5%	RR 2.5%-97.5%	RR 2.5%-97.5%	RR 2.5%-97.5%	RR 2.5%-97.5%	RR 2.5%-97.5%	RR 2.5%-97.5%
Mother Swiss	ZH+ZG+SH	1.15 [0.96-1.39]	1.05 [0.79-1.4]	0.97 [0.76-1.23]	1.05 [0.75- 1.46]	1.54 [1.08-2.2]	1.42 [0.84-2.39]	1.05 [0.58-1.9]
	BE	0.87 [0.66-1.13]	0.83 [0.55-1.23]	0.84 [0.62-1.14]	0.61 [0.36- 1.05]	1.46 [0.63-3.35]	1.39 [0.52-3.75]	0 674239e+62]
	LU	0.68 [0.44-1.06]	0.57 [0.26-1.26]	0.67 [0.4-1.12]	0.26 [0.06- 1.07]	1.49 [0.53-4.19]	0.67 [0.09-5.27]	1.42 [0.4-5.02]
	UR+OB+GL+GR	1.34 [0.87-2.06]	1.18 [0.63-2.21]	1.5 [0.92-2.45]	1.43 [0.74- 2.75]			
	SZ+NW	1.36 [0.79-2.34]	1.77 [0.92-3.41]	1.38 [0.7-2.72]	2.31 [1.06- 5.01]	1 [1-1]	1 [1-1]	1 [1-1]
	FR	1.41 [1-1.98]	1.83 [1.17-2.88]	1.56 [1.04-2.35]	1.33 [0.71- 2.48]	0.9 [0.19-4.18]	1.98 [0.39-9.99]	1.15 [0.14-9.58]
	SO+JU	1.26 [0.83-1.92]	1.42 [0.75-2.67]	1.43 [0.86-2.38]	1.82 [0.87- 3.83]			
	BS+BL	0.87 [0.6-1.26]	0.76 [0.42-1.35]	0.76 [0.47-1.23]	0.49 [0.18- 1.31]	1.22 [0.67-2.24]	1.11 [0.5-2.45]	1.12 [0.46-2.69]
	AR+AI+SG	0.96 [0.67-1.37]	1.17 [0.71-1.93]	1.07 [0.69-1.67]	1.58 [0.84- 2.99]	0 85016e+100]	1 [1-1]	1 [1-1]
	AG	1.31 [0.97-1.76]	0.92 [0.56-1.51]	1.19 [0.83-1.72]	0.81 [0.43- 1.51]			
	TG	1.12 [0.69-1.8]	1.39 [0.74-2.62]	1.31 [0.76-2.26]	1.43 [0.57- 3.56]	1.3 [0.28-6.09]	2.7 [0.58-12.63]	3.2 [0.63-16.24]
	TI	0.98 [0.6-1.62]	0.78 [0.38-1.61]	0.69 [0.38-1.25]	0.61 [0.25- 1.45]	0.42 [0.09-1.88]	0 961234e+86]	0.42 [0.09-1.88]
	VD	0.9 [0.68-1.19]	0.8 [0.52-1.25]	1.01 [0.72-1.41]	0.9 [0.53- 1.54]	1.24 [0.57-2.71]	0.68 [0.2-2.34]	1.77 [0.73-4.26]
	VS	0.99 [0.67-1.45]	1.17 [0.69-2]	0.77 [0.47-1.28]	1.18 [0.61- 2.26]	1.77 [1.03-3.06]	2.54 [1.4-4.61]	1.94 [1.05-3.56]
	NE	0.85 [0.44-1.63]	0.55 [0.19-1.6]	0.92 [0.42-2]	0.45 [0.1- 1.99]	0 94405e+107]	0 54233e+126]	0 57646e+123]
	GE	1.05 [0.74-1.49]	1.22 [0.71-2.12]	0.95 [0.63-1.43]	1.8 [0.9 -3.59]	0.85 [0.53-1.37]	1.3 [0.75-2.25]	0.92 [0.53-1.6]
Mother not Swiss	ZH+ZG+SH	1.15 [0.95-1.39]	1.06 [0.8-1.41]	0.96 [0.76-1.22]	1.05 [0.75-1.47]	1.57 [1.1-2.24]	1.49 [0.88-2.5]	1.11 [0.62-2.01]
	BE	0.87 [0.67-1.14]	0.82 [0.55-1.23]	0.84 [0.62-1.14]	0.62 [0.36-1.05]	1.46 [0.64-3.35]	1.38 [0.51-3.72]	0 451295e+61]
	LU	0.61 [0.39-0.98]	0.55 [0.23-1.29]	0.58 [0.33-1.01]	0.29 [0.07-1.2]	1.7 [0.59-4.89]	0.89 [0.11-7.48]	1.88 [0.5-7.01]
	UR+OB+GL+GR	1.28 [0.82-2]	1.23 [0.66-2.3]	1.41 [0.86-2.33]	1.45 [0.75-2.8]			
	SZ+NW	1.35 [0.78-2.35]	1.87 [0.98-3.55]	1.3 [0.65-2.63]	2.46 [1.14-5.29]	1 [1-1]	1 [1-1]	1 [1-1]
	FR	1.46 [1.03-2.06]	1.91 [1.22-3]	1.64 [1.09-2.47]	1.42 [0.76-2.67]	0.94 [0.2-4.4]	2.37 [0.45-12.55]	1.79 [0.19-17.28]
	SO+JU	1.26 [0.83-1.93]	1.4 [0.74-2.65]	1.42 [0.85-2.37]	1.77 [0.83-3.77]			
	BS+BL	0.86 [0.6-1.25]	0.75 [0.42-1.34]	0.75 [0.47-1.21]	0.49 [0.18-1.31]	1.22 [0.67-2.22]	1.11 [0.5-2.44]	1.11 [0.46-2.65]
	AR+AI+SG	0.98 [0.68-1.4]	1.22 [0.74-2.02]	1.1 [0.71-1.72]	1.58 [0.84-2.99]	0 71045e+100]	1 [1-1]	1 [1-1]
	AG	1.28 [0.95-1.73]	0.9 [0.55-1.48]	1.13 [0.78-1.63]	0.77 [0.41-1.45]			
	TG	1.24 [0.77-2.01]	1.5 [0.79-2.85]	1.52 [0.87-2.66]	1.36 [0.55-3.38]	1.26 [0.26-6.02]	2.54 [0.53-12.1]	3.03 [0.59-15.69]
	TI	0.98 [0.59-1.61]	0.79 [0.38-1.61]	0.68 [0.37-1.24]	0.62 [0.26-1.46]	0.43 [0.09-1.95]	0 128058e+83]	0.43 [0.09-1.95]
	VD	0.9 [0.68-1.19]	0.81 [0.52-1.26]	1.01 [0.72-1.42]	0.91 [0.53-1.54]	1.25 [0.57-2.72]	0.69 [0.2-2.35]	1.79 [0.74-4.32]
	VS	1.02 [0.69-1.49]	1.26 [0.74-2.14]	0.8 [0.49-1.32]	1.26 [0.66-2.4]	1.79 [1.02-3.12]	2.6 [1.43-4.74]	1.96 [1.05-3.65]
	NE	0.77 [0.37-1.58]	0.56 [0.19-1.64]	0.9 [0.39-2.07]	0.47 [0.1-2.16]	0 25565e+115]	0 70912e+136]	0 65632e+132]
	GE	1.05 [0.74-1.49]	1.23 [0.7-2.13]	0.95 [0.63-1.43]	1.8 [0.89-3.62]	0.85 [0.53-1.37]	1.3 [0.75-2.24]	0.92 [0.53-1.58]

Table S 2. Relative risk (RR) when exposed to all definitions of heatwaves used in this study. Results are divided into two sub-categories: mothers with Swiss citizenship vs mothers with no Swiss citizenship. The results are shown per canton.

Population	Canton	90th percentile, 2 days		95th percentile, 2 days		90th percentile, 3 days		95th perncentile, 3 days		HI ≥ 90, 2 days		HI ≥ 93, 2 days		HI ≥ 90, 3 days	
		RR	2.5%-97.5%	RR	2.5%-97.5%	RR	2.5%-97.5%	RR	2.5%-97.5%	RR	2.5%-97.5%	RR	2.5%-97.5%	RR	2.5%-97.5%
Mother above 31	ZH+ZG+SH	1.15	[0.96-1.39]	1.06	[0.79-1.41]	0.97	[0.76-1.23]	1.05	[0.75-1.47]	1.26	[0.94-1.7]	1.06	[0.68-1.65]	1.22	[0.77-1.95]
	BE	0.87	[0.66-1.13]	0.82	[0.55-1.22]	0.84	[0.62-1.14]	0.61	[0.36-1.04]	0.87	[0.47-1.63]	0.53	[0.22-1.3]	0.62	[0.15-2.57]
	LU	0.68	[0.44-1.06]	0.57	[0.26-1.26]	0.67	[0.4-1.12]	0.26	[0.06-1.07]	0.34	[0.1-1.12]	0.32	[0.04-2.43]	0.44	[0.1-1.87]
	UR+OB+GL+GR	1.33	[0.86-2.06]	1.19	[0.64-2.22]	1.48	[0.91-2.4]	1.45	[0.76-2.79]						
	SZ+NW	1.23	[0.69-2.19]	1.77	[0.92-3.42]	1.26	[0.62-2.56]	2.33	[1.07-5.08]	1	[1-1]	1	[1-1]	1	[1-1]
	FR	1.39	[0.98-1.96]	1.8	[1.15-2.82]	1.52	[1.01-2.28]	1.34	[0.72-2.5]	1.3	[0.47-3.59]	2.43	[0.75-7.86]	0.67	[0.09-5.15]
	SO+JU	1.28	[0.84-1.95]	1.43	[0.76-2.7]	1.44	[0.86-2.4]	1.84	[0.87-3.88]						
	BS+BL	0.86	[0.6-1.25]	0.75	[0.42-1.34]	0.75	[0.47-1.21]	0.48	[0.18-1.29]	0.84	[0.5-1.43]	0.78	[0.39-1.55]	0.75	[0.36-1.57]
	AR+AI+SG	0.97	[0.68-1.39]	1.18	[0.72-1.95]	1.07	[0.69-1.67]	1.54	[0.82-2.91]	0	[0-5.11e+58]	1	[1-1]	1	[1-1]
	AG	1.28	[0.95-1.73]	0.9	[0.54-1.47]	1.15	[0.79-1.66]	0.78	[0.42-1.45]						
	TG	1.13	[0.7-1.82]	1.37	[0.73-2.57]	1.33	[0.77-2.3]	1.36	[0.54-3.39]	1.82	[0.56-5.83]	2.88	[0.8-10.33]	2.78	[0.74-10.39]
	TI	0.98	[0.6-1.61]	0.79	[0.38-1.62]	0.69	[0.38-1.25]	0.61	[0.26-1.46]	0.44	[0.15-1.28]	0.62	[0.08-4.68]	0.44	[0.15-1.28]
	VD	0.9	[0.68-1.19]	0.81	[0.52-1.25]	1	[0.72-1.41]	0.9	[0.53-1.53]	1.33	[0.67-2.65]	0.9	[0.31-2.63]	1.74	[0.74-4.11]
	VS	0.99	[0.68-1.45]	1.23	[0.72-2.09]	0.77	[0.47-1.27]	1.23	[0.64-2.36]	0.89	[0.55-1.44]	1.06	[0.61-1.84]	0.88	[0.52-1.5]
	NE	0.87	[0.45-1.68]	0.55	[0.19-1.6]	0.92	[0.43-2]	0.42	[0.09-1.89]	0.35	[0.04-2.91]	0733017e+99]		0257587e+97]	
	GE	1.05	[0.74-1.48]	1.24	[0.72-2.15]	0.96	[0.63-1.45]	1.79	[0.9-3.57]	0.82	[0.52-1.28]	1.13	[0.66-1.95]	0.84	[0.49-1.46]
Mother below 31	ZH+ZG+SH	1.15	[0.96-1.39]	1.07	[0.8-1.42]	0.97	[0.76-1.23]	1.06	[0.75-1.47]	1.16	[0.75-1.79]	1.03	[0.52-2.02]	0.63	[0.26-1.5]
	BE	0.87	[0.67-1.14]	0.82	[0.55-1.23]	0.84	[0.62-1.15]	0.61	[0.36-1.04]	0.85	[0.39-1.89]	1.18	[0.49-2.88]	0.53	[0.07-4.09]
	LU	0.68	[0.44-1.05]	0.62	[0.28-1.38]	0.67	[0.4-1.12]	0.29	[0.06-1.07]	1.59	[0.66-3.84]	1.61	[0.37-6.96]	0.72	[0.17-3]
	UR+OB+GL+GR	1.33	[0.86-2.05]	1.21	[0.65-2.26]	1.48	[0.91-2.42]	1.46	[0.76-2.79]						
	SZ+NW	1.53	[0.89-2.64]	1.96	[1.02-3.76]	1.54	[0.77-3.07]	2.48	[1.07-5.08]	1	[1-1]	1	[1-1]	1	[1-1]
	FR	1.48	[1.05-2.1]	1.89	[1.2-2.98]	1.63	[1.08-2.45]	1.35	[0.72-2.5]	2.62	[0.98-6.99]	2.71	[0.7-10.58]	1.71	[0.18-15.95]
	SO+JU	1.23	[0.8-1.88]	1.35	[0.71-2.56]	1.37	[0.82-2.3]	1.73	[0.87-3.88]						
	BS+BL	0.86	[0.6-1.25]	0.76	[0.42-1.36]	0.76	[0.47-1.22]	0.5	[0.18-1.29]	0.86	[0.44-1.66]	0.83	[0.36-1.91]	0.63	[0.23-1.73]
	AR+AI+SG	0.96	[0.67-1.38]	1.18	[0.71-1.95]	1.08	[0.69-1.69]	1.6	[0.82-2.91]	0378172e+77]		1	[1-1]	1	[1-1]
	AG	1.33	[0.99-1.79]	0.93	[0.57-1.54]	1.19	[0.83-1.72]	0.83	[0.42-1.45]						
	TG	1.18	[0.73-1.91]	1.38	[0.73-2.61]	1.39	[0.8-2.4]	1.32	[0.54-3.39]	1.55	[0.34-7.1]	2.54	[0.55-11.66]	2.9	[0.6-13.97]
	TI	0.97	[0.58-1.63]	0.81	[0.39-1.68]	0.65	[0.35-1.22]	0.61	[0.26-1.46]	1.11	[0.3-4.19]	088761e+115]		1.12	[0.3-4.22]
	VD	0.9	[0.68-1.19]	0.8	[0.52-1.25]	1.01	[0.72-1.42]	0.91	[0.53-1.53]	0.6	[0.25-1.45]	0.83	[0.29-2.38]	0.72	[0.25-2.04]
	VS	1	[0.68-1.47]	1.27	[0.74-2.15]	0.78	[0.47-1.29]	1.26	[0.64-2.36]	1.26	[0.81-1.96]	1.58	[0.95-2.62]	1.34	[0.83-2.16]
	NE	0.88	[0.45-1.7]	0.52	[0.18-1.52]	0.98	[0.45-2.17]	0.41	[0.09-1.89]	0.62	[0.07-5.43]	1.28	[0.13-12.5]	1.06	[0.11-10]
	GE	1.05	[0.74-1.48]	1.22	[0.7-2.13]	0.94	[0.62-1.43]	1.81	[0.9-3.57]	1.2	[0.7-2.05]	1.69	[0.9-3.17]	1	[0.52-1.94]

Table S 3. Relative risk (RR) when exposed to all definitions of heatwaves used in this study. Results are divided into two sub-categories: mothers above 31 years vs mothers below 31 years. The results are shown per canton.

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Declaration of consent

on the basis of Article 30 of the RSL Phil.-nat. 18

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Title of the thesis: Heatwaves and preterm birth in Switzerland

Supervisor: Dr. Ana Maria Vicedo-Cabrera

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