CS Healthcare Database

CREDIT SUISSE

Therapeutic Journeys in diabetes

Authors

European Pharma Team
44 207 888 0304
creditsuisse.pharmateam@credit-suisse.com

Dominic Lunn
44 20 7883 0471
dominic.lunn@credit-suisse.com

Harry Sephton, CFA
44 20 7883 5285
harry.sephton@credit-suisse.com

Elizabeth Walton
44 20 7883 9767
elizabeth.walton@credit-suisse.com

Jo Walton
44 20 7888 0304
jo.walton@credit-suisse.com

Matthew Weston PhD
44 20 7888 3690
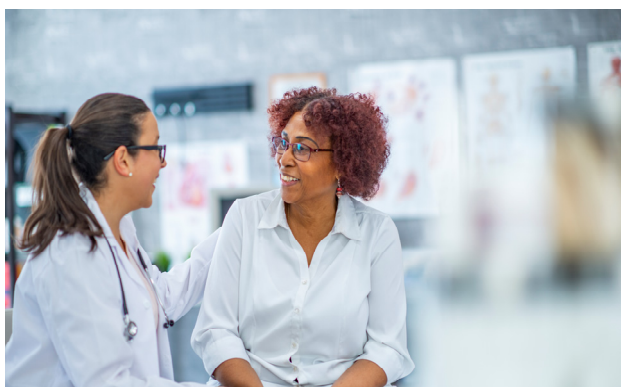matthew.weston@credit-suisse.com

Matt Miksic
212 325 4381
matt.miksic@credit-suisse.com

Contents

A letter from the Global Head of Securities Research

To our valued institutional clients and to the medical community,

In this report we draw for the first time from our new CS Healthcare Database, marking a new phase of our roughly 4-year journey into alternative data. As a core component of our alternative data initiative, we were provided access to a database that includes anonymized prescription and medical claims records from a population of roughly 120 million US people, which we refer to as the CS Healthcare Database. In total we analyzed billions of records using a seasoned team of data scientists and a world class team of pharmaceutical sector experts. Our data assets themselves are sourced through strategic partnerships with global companies.

In the report that follows, we used a mosaic of inputs to create representative patient journeys in diabetes. With this data, we also assessed treatment choices as a function of effectiveness, brand loyalty, compliance, and financial burden. We hope the broader medical community, in addition to our traditional financial community clients, find our work helpful and engage with us on future projects.

We are thrilled to begin enhancing our Research product with the unique signals available from our alternative data effort and we look forward to introducing new capabilities across a wide variety of healthcare topics, as well as coverage of a myriad of sectors.

Thanks and enjoy!

David Bleustein, Global Head of Securities Research

Executive summary

Proprietary database accessing prescription and medical claims records of around 120m US citizens. This allows us to follow patient journeys assessing treatment choices with contextual data such as funding status. Claims for drugs delivered in a hospital or in a doctor's office are not well covered by other audit services.

We introduce our proprietary Credit Suisse Healthcare Database with our first analysis being a deep dive into the US Type 2 diabetes market. Our US database contains anonymised claims data for over 60m US citizens from a subscriber database of more than 120m people, representative of overall US demographics and income levels. It includes over 2.4bn prescription (Rx) claims and over 6.8bn medical claims (Mx) from 2017 to end-2021 across all diseases and provides an opportunity to view the usage of many physician office and hospital-based drugs that are not clearly articulated in other US audit data. The ability to follow patients over time gives us a unique opportunity to assess treatment choices, persistence of treatment, the use of drug cocktails, and likely follow-on choices.

Our key diabetes insights include the following:

- Typically >10% abandonment of prescriptions after only one claim, and 25-30% abandonment by month 4. Our database shows real-world median persistence of c.27 months for Trulicity and Ozempic. Data from a 2015 Trulicity cohort shows a mean stay time of c.40 months versus Novo Nordisk's claims of c.50 months for weekly GLPs.

- Growing metformin use, especially in younger patients, indicates likely strong future category growth as early patients today progress and need to intensify treatment. More than 50% of patients use drug cocktails, many of which include two brands.

- GLP adoption is rising in all ages and funding channels. GLP adoption is similar in commercial and government channels; however, the mix within GLPs shows higher use of Ozempic in commercial channels and a higher use of Trulicity and Victoza in government channels. Medicare expansion to cover 61- to 65-year-olds could see 4% lower Ozempic volumes if coverage did not change.

The proprietary Credit Suisse Healthcare Database covers one-third of the US population. It offers a unique insight into the treatment of various diseases in the United States. The full database contains health care claims covering both outpatient prescriptions and medical procedures from more than 120m US citizens. This is based on medical claims filed for insurance purposes across both commercial and government channels. Although we have limited data from 2012, we concentrate our analysis on trends starting in 2017. Over this period, the database increased from coverage of 114.5m active subscribers to 121.9m. Of these, an increasing proportion have made Rx or Mx claims. Our data has c.51m of plan subscribers submitting claims in 2017, rising to c.62m in 2021. This sample covers around one-third of the US population for Rx claims and somewhat less for Mx claims.

This database allows us to follow typical therapeutic journeys through a disease. It allows us to view persistence on a therapy, compliance with a therapy, common treatment cocktails, and transitions onto and off specific drugs. The database contains both medical and prescription claims, so we can see claims for drugs delivered in both office/hospital settings and those given in outpatient settings in an equivalent fashion. We have visibility into quantities of drug per Rx, and access to co-pay details for drugs, although not for medical claims.

Co-pay data allows us to look at the 'financial toxicity' of treatments. Persistence and compliance to therapy allow us to judge market penetration better.

Medical claims made under a permanent J code can also be analysed, although any associated diagnosis codes must also have been completed diligently to provide context. This adds some specialty pharmacy drugs that are often excluded in other audit services. However, claims for new drugs logged under a temporary J code will not be captured, limiting utility to trends in established drugs given in an office setting.

This data is most useful when looking at longer-term trends. As the data within the Credit Suisse Healthcare Database is drawn from claims, and is not sampled at the point of delivery, we do see a lag versus other services for Rx data. There is a longer lag between service date and reporting for medical claims as opposed to traditional Rx claims.

We initiated our use of this database looking at the Type 2 diabetes market, as this is an important growth area and one where there is much debate over the relative strengths of both different classes of drugs and in particular between the leading GLP-1 drugs. Within the overall database of c.122m citizens in 2021, we have isolated the c3m who have made annual claims for specific diabetic medications and reviewed their use of medications over time. CDC data estimates that c8.7% of the US population have diagnosed diabetes. This data set implies that c30% of US diabetes patients receive treatment. *We note that the absolute number of patients with a diabetes-related claim (Rx and Mx) decreased over the 2017-2021 period (from 3.04m to 2.88m), despite a rise in the number of overall claims and overall subscribers. We do not believe this can be explained by a change in the underlying health of the subscriber database. We have not analysed enough other disease areas to see if this is a more general finding.*

Despite apparently low numbers of diabetes medication claimants, the overall data set shows a broad agreement on levels of prescribing and implied company sales for outpatient drugs with other audit services, with no obvious distortion in diabetes from formulary positioning from plan sponsors. An exception is the 1Q20 COVID-19 stockpiling, which our methodology of counting days on therapy as opposed to time and value of scripts did not capture.

For each drug, we provide a Credit Suisse Healthcare Database profile detailing the count of patients on each drug, a view of transitions onto and off the drug for 2021, and time on treatment analysis. We also provide a snapshot of current use by age and funding channel and report the trend in patient co-pay.

Figure 1: Credit Suisse Healthcare Database: Insights from US healthcare claims

Year	Overall Subscribers	Subscribers	Subscribers with claims	Overall Claimants			Diabetes Claimants		
				Rx	Mx	of which Rx & Mx	Rx	Mx	of which Rx & Mx
2017	114.5	105.8	50.7	31.6	20.7	15.3	3.04	1.83	1.22
2018	112.3	104.1	53.0	32.3	20.3	15.0	2.40	1.72	1.18
2019	118.1	103.9	57.9	33.4	21.6	15.3	3.06	1.80	1.20
2020	111.2	103.0	61.2	36.0	20.4	15.0	3.20	1.71	1.21
2021	121.9	113.1	61.9	43.6	20.3	15.6	2.88	1.33	0.96

Source: Credit Suisse Healthcare Database (Rx claims = prescription claims, Mx claims = medical claims)

" The majority of patients take more than one drug for their diabetes and rates of abandonment after only one claim are high.

Diabetes key conclusions

Increasing use of metformin in younger cohorts in the US suggests earlier diagnosis of type 2 diabetes. This suggests diabetes will continue to be a fast growing disease as patients intensify treatment over time. The majority of patients take more than one drug for their diabetes and rates of abandonment after only one claim are high. In this real world setting we see a 50% drop off on treatment in 13-16 months despite the chronic nature of the diseases.

- **Metformin single-agent use increasing, suggesting more patients entering treatment.** With more patients starting initial treatment at an earlier age, we expect patients to need more intensive treatment before the age of 65, when many patients transition to Medicare plans that still typically look to use a higher proportion of generic versus branded drugs.

- We see a clear lead in the GLP segment developing for Ozempic. Whilst Trulicity remains the leading drug in the class in CS database total claims, and in IQVIA scripts in 2021, we see a clear lead for new patients developing for Ozempic from June 2021. Within the SGLT-2 class, we see growing new patient share for Farxiga but Jardiance retains dominance.

- **Drug cocktails prevalent and add to costs.** Over 50% of use in diabetes is via drug cocktails. An SGLT-2 (Farxiga) + weekly GLP (Trulicity) combo in a commercial setting would cost a patient around $78 per month today. The number of patients taking SGLT-2-containing combos has risen 34% over the past five years, with a 30% decline in DPP-4 combos. (*See Appendix 1 for details on the key drug classes in diabetes.*)

- **'Financial toxicity' analysis shows limited barriers to GLP-1 adoption.** Our analysis of co-pays shows an expected premium for the newer GLP-1 therapies; however, the co-pay premium to other branded treatments was only 11% in 2021 and has been trending down since 2017 and hence we do not see this as a significant barrier to treatment.

- **GLP-1 adoption is similar in government and commercial channels.** There is no material difference in GLP-1 adoption in over-65 Medicare patients vs in over-65 commercial patients; therefore, we would not expect any material changes to class market-share dynamics if Medicare were expanded to over-60s.

However, within GLPs, Ozempic has a higher share of commercial channels, and the older GLPs, Trulicity and Victoza, have a higher relative share in government channels. We see higher rebating in Trulicity and Victoza (Figure 85), which could be due to higher rebating for favourable formulary access in government channels.

- **Co-morbidities unlikely to impact uptake of branded diabetes drugs.** A review of claims outside of diabetes for the diabetes cohort indicates no higher incidence of heart disease than in an age-matched non-diabetic cohort, nor widespread use of other Rx brands that could limit trade-up to diabetes brands.

- **Time on treatment shows high level of abandonment.** We see >10% abandonment after the first claim (typically for one month of treatment) and typically 25-30% abandonment by Month 4. In this real-world setting, we do not see the c.50-month stay time reported by Novo for Ozempic or Trulicity but see a 50% drop-off in 13-16 months. Counting treatment only from Month 4 we see a 50% drop-off in the 27-month range. We see no difference between Trulicity and Ozempic in persistence. Trulicity data for a cohort of patients who started treatment in 2015, who were still active in the database in 2021 with 85 months of claims data, indicates a mean stay time of c.40 months. We will look to examine stay time further as we review different therapy areas to see if we can gain more insights into this finding.

- **Overall compliance of 79%, but with a range from 70% for Tresiba to over 80% for DPP-4s and SGLT-2s.** This is measured by the percentage of actual claims over expected claims for continuous treatment. Rybelsus is also high at 82%, suggesting that there are no issues with fasting, but the sample size is quite low. We see slightly higher compliance for Trulicity (74%) than for Ozempic (71%).

“ Drug cocktails are prevalent and add to costs.

CS Healthcare Database: Diabetes analysis

The database highlights growing use of SGLT-2s versus DPP-4s. It also highlights growing use of GLP-1s and a shift from Trulicity to Ozempic in new patient starts.

Growing use of Ozempic over Trulicity

The CS Healthcare Database allows us to track drug use for new and established patients over time. In the data sets below, please note that the CS data is monthly with a cut-off in December 2021, but the IQVIA data is weekly and runs to 11 March 2022. In Figure 2, we compare the trends in the total number of claimants for various GLP-1 drugs with IQVIA TRx data shown in Figure 3.

In Figure 4, we show the monthly new patient count. In this analysis, we count patients who have not claimed for the specific brand before (or who have not made such a claim for at least eight months previously). The spike of new patients each January reflects new enrollees to the database. Here we compare this data with weekly New to

Brand data (NBRx) from IQVIA in Figure 5. This data set clearly shows the strength of Ozempic over Trulicity in new patient starts.

Jardiance still dominates the SGLT market

In Figure 6 to Figure 9, we repeat the comparison with drugs in the SGLT-2 class. We note that in the CS database, Invokana appears to be used more frequently and Steglato less frequently than is evident from the IQVIA database.

In Figure 10 and Figure 11, we look at established patient trends in both drug classes, counting only patients who are at least 70% compliant with expected treatment levels as measured by number of days of therapy claimed. There is no equivalent readily available IQVIA data set.

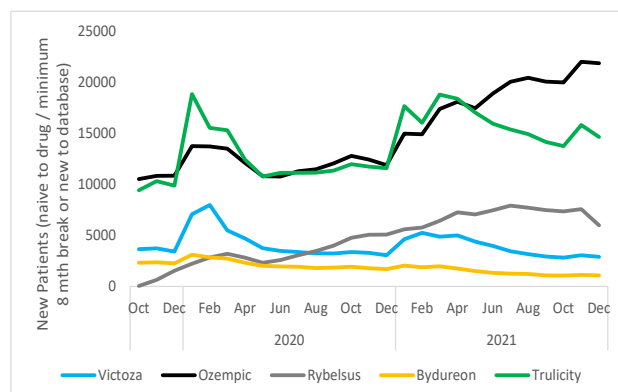**Figure 2: CS database total patient count GLPs**
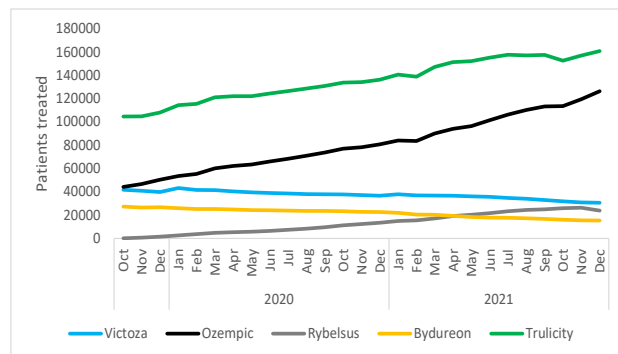
Source: Credit Suisse Healthcare Database
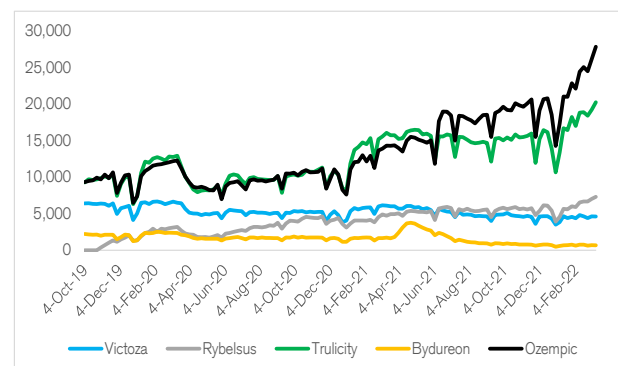
Figure 3: IQVIA TRx data GLPs
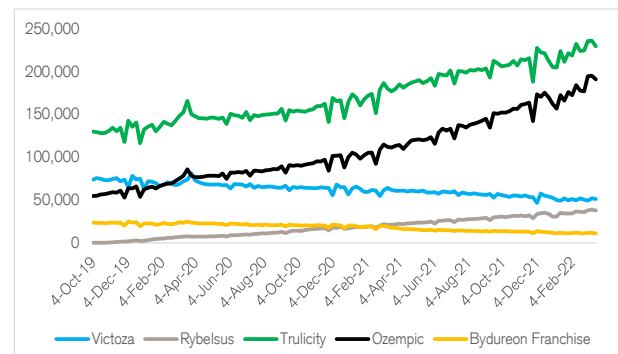
Source: IQVIA audit data

Figure 4: CS database new patient count GLPs

Source: Credit Suisse Healthcare Database
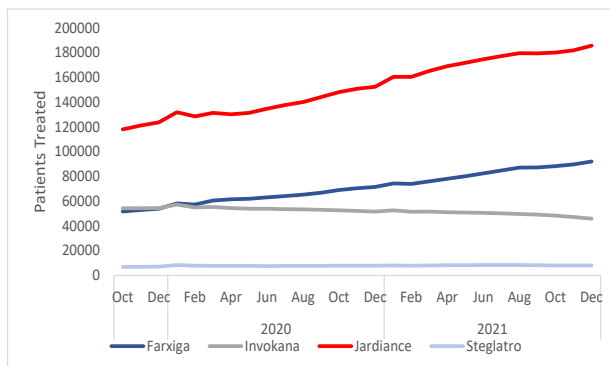
Figure 5: IQVIA NBRx data GLPs

Source: IQVIA audit data

Metformin single-agent use increasing, suggesting more patients entering treatment

- We have identified higher use of metformin single-agent therapy, with growing use of this drug in younger patients. This could reflect earlier intervention in the disease, or a greater incidence of Type 2 diabetes in younger patients which will be sustained as this cohort ages.

- With more patients starting initial treatment at an earlier age, we expect patients to need more intensive treatment before the age of 65, when many patients transition to Medicare plans that still typically look to use a higher proportion of generic versus branded drugs.

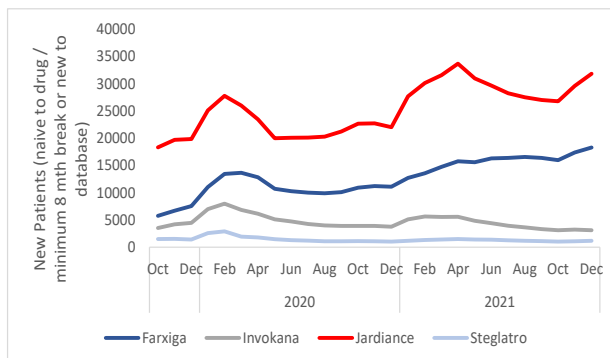**Figure 6: CS database total patient count SGLT-2s**

Source: Credit Suisse Healthcare Database
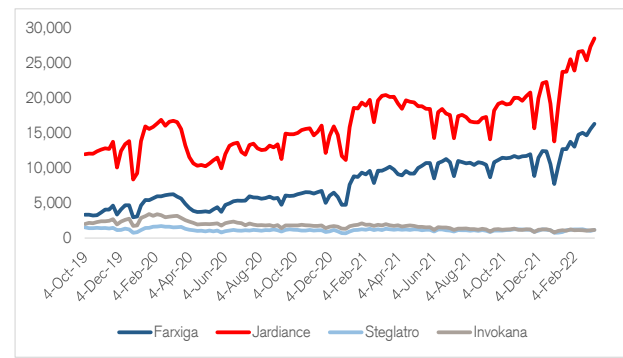
Figure 7: IQVIA TRx data SGLT-2s
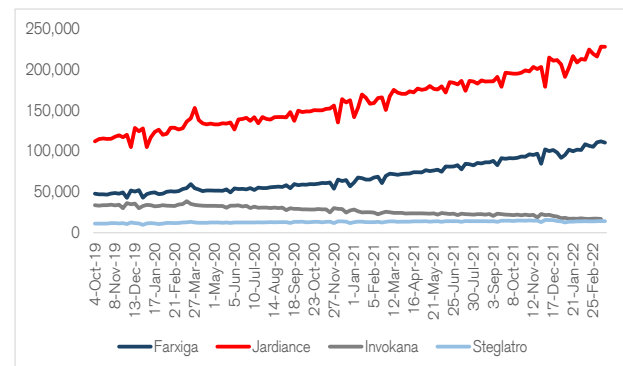
Source: IQVIA audit data

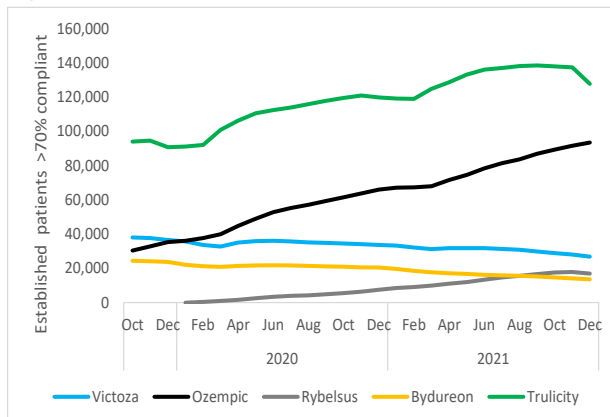**Figure 8: CS database new patient count SGLT-2s**

Source: Credit Suisse Healthcare Database

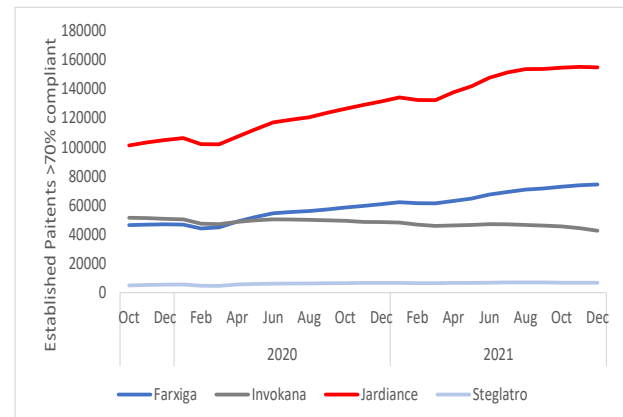**Figure 9: IQVIA NBRx data SGLT-2s**

Source: IQVIA audit data

Figure 10: CS database established patient count GLPs

Source: Credit Suisse Healthcare Database

Figure 11: CS database established patient count SGLT-2s

Source: Credit Suisse Healthcare Database

The Credit Suisse Healthcare Database shows that the count of prescriptions for metformin for single-agent use (as monotherapy) over the 2017-2021 period increased by 15%. When we look at the absolute number of patients on metformin in 2021 versus 2017, we see only a 2% increase in unique patients but a 12% increase in total prescriptions.

Looking at the breakdown of patients by age cohort, we see that the increase is not uniform across age groups. Use of metformin in the 17-25-year group and 26-45-year group increased 45% and 23%, respectively, from 2017 to 2021. However, use in the older cohorts remained broadly stable.

Drug cocktails prevalent and add to costs

- Over 50% of use in diabetes is via drug cocktails. The number of patients taking SGLT-2-containing combos has risen 34% over the past five years, with a 30% decline in DPP-4 combos.

- Jardiance remains the leading SGLT-2, both in mono and combo therapy. An SGLT-2 (Jardiance) + weekly GLP (Trulicity) combo in a commercial setting would cost a patient around $78 per month today, down from $94 in 2017 before any manufacturer co-pay assistance.

- Given the widespread use of cocktails, we see an opportunity for Rybelsus as a new oral GLP to be switched into combos that currently combine both oral and injectable drugs. Rybelsus has a monthly commercial co-pay of c$47 against $41 for Trulicity.

- GLP-1 shows a 13% premium in co-pay to other treatments, although this has fallen from 25% a few years ago.

A key benefit of being able to track an individual patient's drug usage is to look at the most common combinations of treatments. This may give us insights into the level of efficacy of individual drugs and the pill and/or cost burden for patients who are taking combinations. For this analysis, we have looked at aggregated drug class data for 2017 and 2021, but some individual drug data is based on 2017 and 2020 data.

We have also looked at the key branded drug classes and reviewed the use of single and combination therapy over time. We assessed each patient for the drugs taken over 2017 and 2021 and have classified patients as taking single medication if that was the predominant prescription in that year. If a patient took more than one combination, we ascribed them to the combination taken for the longest time period over the year. If we include metformin monotherapy, then overall combos are c.50% of treatment; if we exclude single-agent metformin use, combinations account for around 80% of the market.

For each of the main branded drugs, we have reviewed the top 10 drug regimens (single agent and combinations). In all cases, the top 10 regimes cover at least 50% of the total use of each drug. We then classified each combination as a branded drug cocktail (that will likely add significant costs to the patients) or as combinations of one brand and one or more generics (which are unlikely to add significantly to costs). We have highlighted those combinations of branded drugs that include insulin, which tends to be added at later stages of the disease. For the long-acting insulin cohort, the "plus insulin" sub-group are those patients that have added a second insulin to the basic insulin drug cocktail within the top 10 specific combinations.

On the right-hand scale of Figure 12 to Figure 19, we have plotted the total number of patients in the Credit Suisse Healthcare Database taking each drug. This data counts patients under each drug they take. Therefore, for example, a patient taking a combination of Januvia plus metformin, the most common branded combination with metformin, will show up in the total patient numbers for both metformin and Januvia in this analysis. The analysis highlights the characteristics of the eight most common cocktails, beyond monotherapy and a simple combination with metformin. Specifically, we highlight those combinations with two branded drugs where the combined monthly co-pay may be a barrier to utilisation.

Figure 12: Use of combinations by class, 2017 to 2021, and by patient numbers (*excluding metformin which is off the scale)
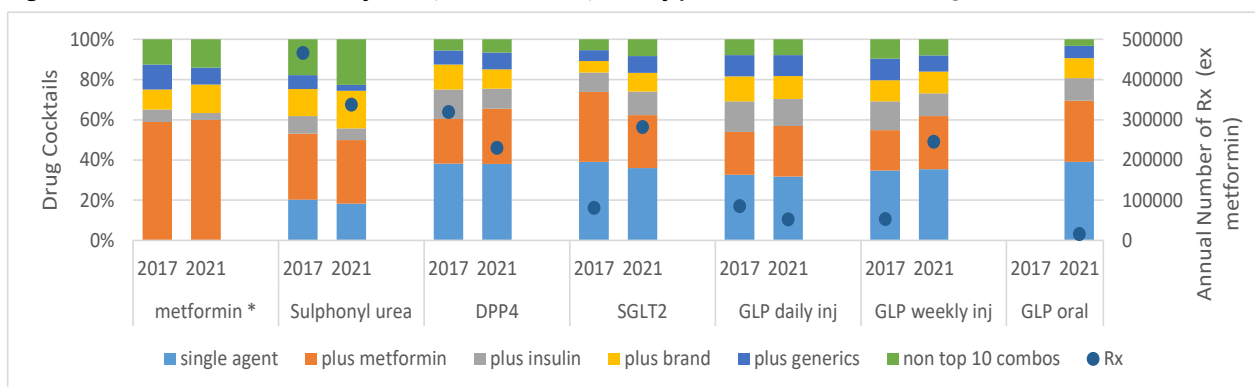
*Note that with c.1.8m patients taking metformin in 2017 and >2.1m in 2021, the number of metformin patients does not fit on this scale.
Source: Company data, Credit Suisse , Credit Suisse Healthcare Database
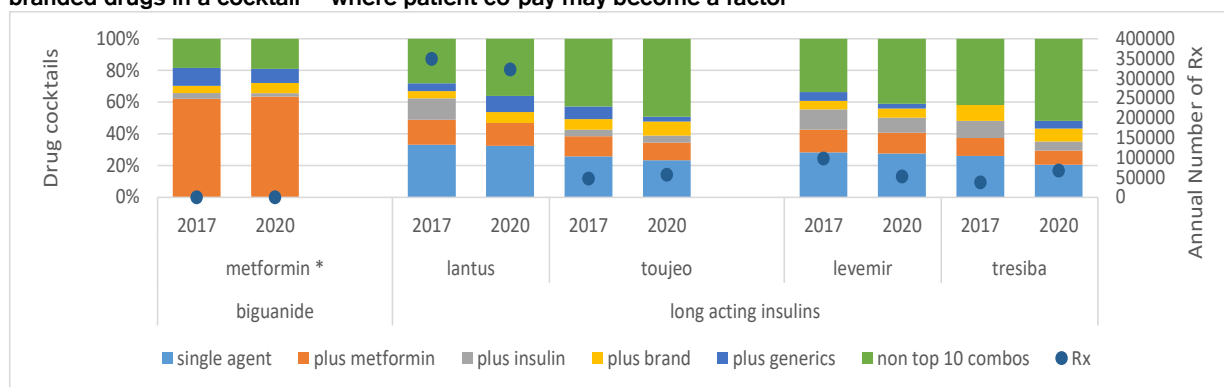
Metformin

Metformin is still the most widely used drug in treating diabetes and was the sole diabetes Rx medicine for 60% of the database in 2021, up slightly from 59% in 2017. Metformin is used as the primary add-on treatment to other branded agents a further c6% of the time. We might have expected single-agent metformin use to be going down over time with the advent of newer classes of drugs. The increase is marked in earlier age cohorts and may reflect either earlier intervention or more widespread prevalence of diabetes.

DPP-4s

We note that DDP-4 use slipped below that of the SGLT-2 class in 2021 when comparing total use of the drug, especially in single-agent use, but that overall use of the class including in popular combinations declined by 28% over 2017 to 2021, in contrast to >200% growth in the use of SGLT-2. DDP-4s may still be being used earlier in treatment when blood sugar is easier to control. The most common brands added to DPP-4 treatment are the SGLT-2s, retaining an all-oral treatment approach.

Figure 13: Use of common drug cocktails with metformin and insulins. We highlight within the top 10 combinations used in each year, the % of use as single agent, the % of metformin combinations, and the level of use of two branded drugs in a cocktail— where patient co-pay may become a factor


*Note that with c.1.8m patients taking metformin in 2017 and >2.1m in 2021, the number of metformin patients does not fit on this scale.
Source: Credit Suisse Healthcare Database

Figure 14: Use of drug cocktails SU, DPP-4 and SGLT-2s: % of use as single agent, combined with metformin and characteristics of the eight most common cocktails
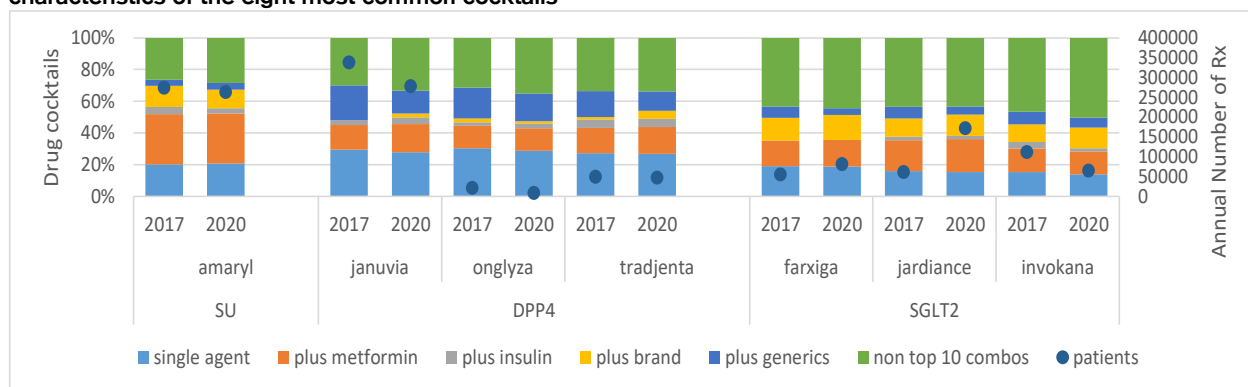
Source: Credit Suisse Healthcare Database

Figure 15: Use of drug cocktails for GLPs: % of use as single agent, combined with metformin and the characteristics of the eight most common cocktails
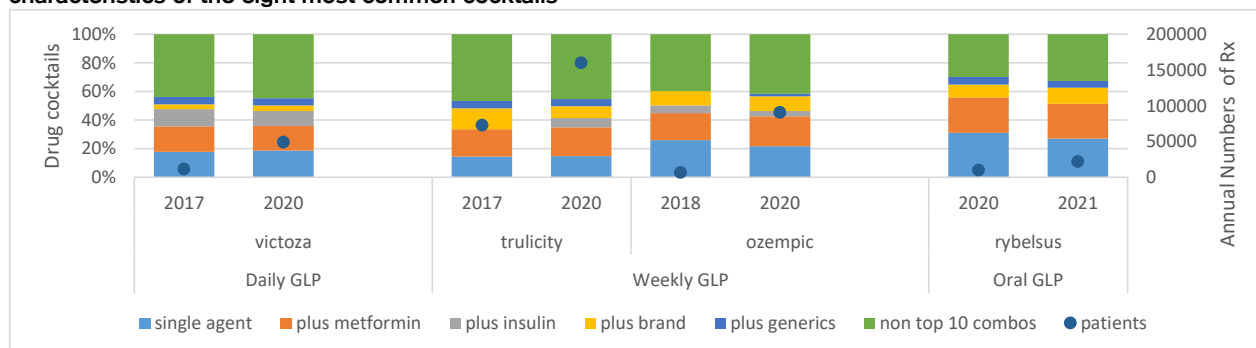
Source: Credit Suisse Healthcare Database

SGLT-2s

The use of SGLT-2s grew strongly, both as single-agent (>200%) and in combination (+300%) from 2017 to 2021. The most common other mechanisms of action combined with the SGLT-2s (after metformin) are the weekly GLP-1s, which combine an oral and injectable treatment. This combination, which adds an injectable GLP to existing oral SGLT-2 treatment, represents a serious intensification of therapy.

As expected, we have seen the SGLT-2 growth led by Jardiance. Growth has come largely at the expense of Invokana, for which our database suggests that single-agent usage has fallen from a 45% share of the class to 17%. Invokana had a black box warning for risk of amputation from 2017 to September 2020; this likely explains its falling popularity in the face of alternative drugs in the same class, including Jardiance, which was the first of the class to gain a cardiovascular protection label back in 2016.

GLP-1s

Within the weekly GLP-1s, we see that Trulicity continued to outpace Ozempic between 2017 and 2021. Ozempic is used as a single agent more often (22% of use versus 14% for Trulicity), although, as expected, a combination with metformin is the most common cocktail used by a further 20% of patients.

Looking at Rybelsus (the only oral GLP-1), in 2021 we saw 23% single-agent use, a further 29% combined with metformin and 8% combined with an SGLT-2. The ninth most common combination accounting for only 2% of 2021 scripts added a basal insulin to the mix.

Given the convenience of oral Rybelsus, we see a significant opportunity to grow the Rybelsus plus SGLT-2 combo for patients who wish to avoid taking regular injectable products.

Cocktail co-pays

In the next section, we look at co-pays but note here the most common cocktail of a DDP-4 (Januvia) + SGLT-2 (Jardiance) would have cost c.$74.48 in co-pay per month in 2021 in a commercial setting, down from $79.24 in 2017. Similarly, an SGLT-2 (Jardiance) + weekly GLP (Trulicity) combo would typically cost $77.42 per month in co-pay in a commercial setting, down from $94.56 in 2017. These commercial co-pays may be lowered by manufacturer assistance programmes (see Figure 85 for US gross-to-net prices for leading diabetes drugs). In a Medicare setting, the patient co-pay of these combos would be $25.73 and $28.46 per month, respectively.

'Financial toxicity' in diabetes: Co-pays are not a significant barrier to GLP-1 adoption

■ Our analysis of co-pays shows an expected premium for the newer GLP-1 therapies; however, the co-pay premium to other branded treatments was only 11% in 2021 and has been trending down since 2017; hence, we do not see this as a significant barrier to treatment.

■ GLP-1 adoption is similar in commercial and government channels, but the share for Ozempic over Trulicity is much higher in commercial than government channels.

■ There is no material difference in GLP-1 adoption in over-65 Medicare patients vs in over-65 commercial patients; therefore, we would not expect any material changes to market-share dynamics if Medicare were expanded to the over-60s. What is clearer from the analysis on treatment demographics is that GLP-1 adoption has been much greater in the 25-65 age bracket than in older and younger populations.

■ Co-morbidities appear unlikely to affect the uptake of branded diabetes drugs. Surprisingly, we saw no higher incidence of patients taking heart disease medication in our diabetes cohort than in an age-matched sample of non-diabetic patients. The vast majority of additional Rx claims were for generics, for which we assume co-pays are limited.

Co-pays can influence patient decisions and time on treatment

The database allows us to track co-pay data by product over time and by payer type (commercial, Medicare, Medicaid). Our analysis of commercial co-pays shows an 11% premium on average for GLP-1 drugs over other branded diabetes therapies, declining from a 24% premium in 2017.

We do not expect this premium to be a hindrance to uptake, with all other branded diabetes therapies (DPP-4s, SGLT-2s, long-acting Insulins) commanding a significant (>10x) co-pay premium to metformin.

Notably, since 2019, co-pays for all diabetes therapies have been in decline, with 2021 average co-pays 13% lower than 2019 for commercial payers, 10% lower for Medicare and 56% lower for Medicaid.

Co-morbidities not a barrier to intensification of therapy

The database allows us to look for co-morbidities and any extra cost burden this may place on patients. To check for this, we compared the overall Rx claims of the 2.9m diabetics with an age-matched group of patients who made at least one Rx claim in 2021 but who had never claimed for any diabetes medications.

■ We were surprised not to see a higher incidence of claims for drugs for heart disease. High blood pressure medication accounted for 13.5% of diabetics vs 15.3% for the non-diabetics claims with a further 1% in both cohorts for heart failure.

■ We saw very few branded drugs prescribed with any frequency, with Synthroid (thyroid hormone), Vyvanse (ADHD), Eliquis and Xarelto (both for stroke prevention in patients with atrial fibrillation) being the only brands that could add a cost burden with likely higher co-pays than generics. We saw no material use of Entresto or other specific drugs for heart failure.

Figure 16: Typical monthly co-pays for classes of drug by funding status
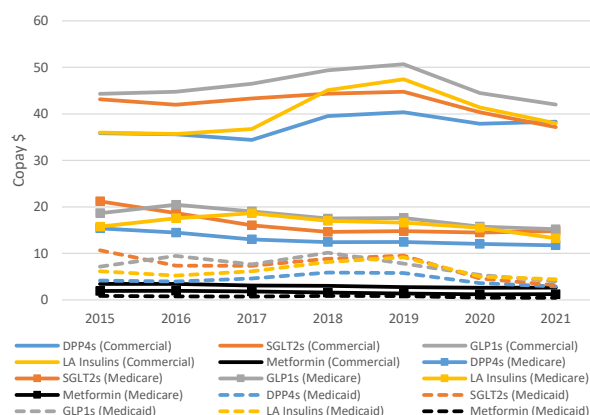
Source: Credit Suisse Healthcare Database

**Figure 17: Commercial co-pay premium for GLPs over other branded classes (ex-metformin)**
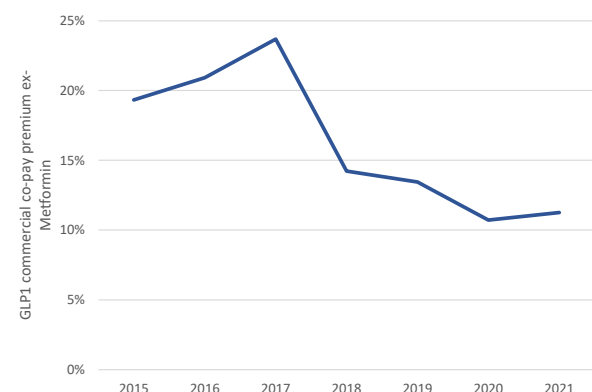
Source: Credit Suisse Healthcare Database

**Demographics data provides key insights into GLP-1 adoption**

■ The database allows us to look at funding demographics for each drug, including split by age and payer type on an annual basis.

■ When looking at the demographics by age, there is clearly lower penetration of GLP-1s in the over-65s and much higher penetration of DPP-4s irrespective of payer type. Government payers account for around 77% of the over-65s diabetes spending.

■ Metformin accounts for the majority of claims in all age groups except 0-16 where insulins are more prevalent. Payer split is relatively similar for metformin, SGLT-2s and GLPs, whereas DPP-4s and insulins have a clearly higher mix of government payers.

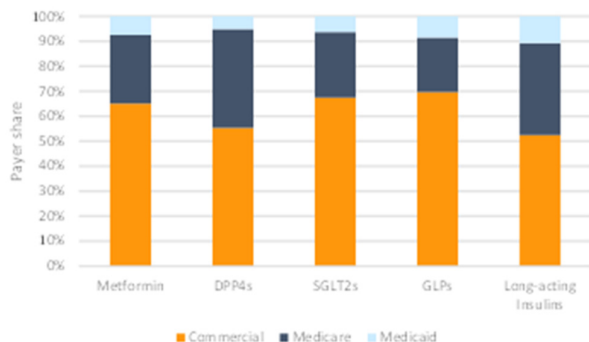**Figure 18: Diabetes treatment split by age in 2021**
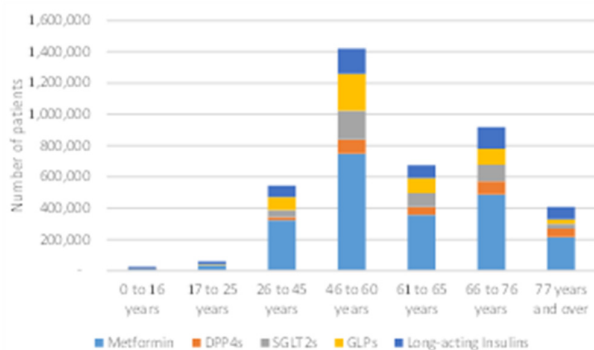
Source: Credit Suisse Healthcare Database
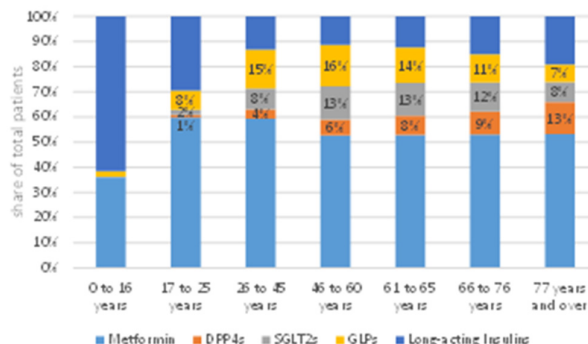
Figure 19: Diabetes payer mix by age group in 2021
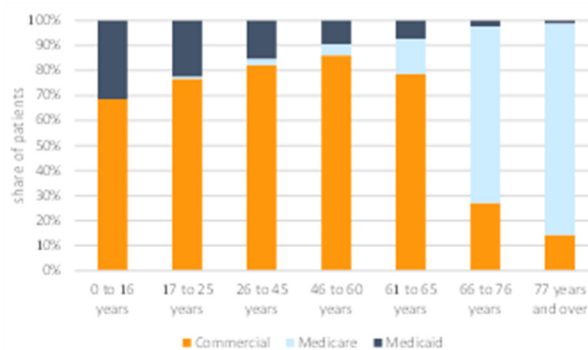
Source: Credit Suisse Healthcare Database

Figure 20: Payer share by therapy class in diabetes

Source: Credit Suisse Healthcare Database

Figure 21: 2021 market share by demographics (all payers)
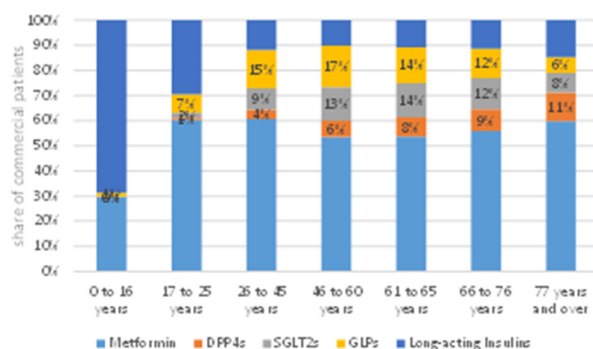

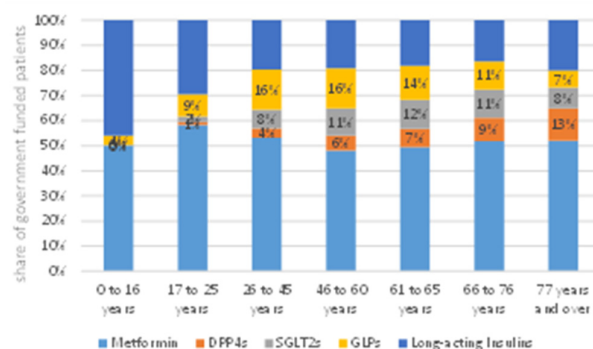Source: Credit Suisse Healthcare Database

16

- Our analysis of the data on GLP-1 treatment shows that the share of patients is similar in both commercial and government channels in over-60s. Hence, we would not expect any material changes to class market-share dynamics if Medicare were expanded to over-60s.

- However, when looking at the share within GLP-1 treatments, the newer therapies, Ozempic and Rybelsus, have seen higher share in commercial payers than seen with government payers, despite apparently lower co-pays for GLP-1s in Medicare as opposed to commercial settings. For Ozempic, this may reflect greater price sensitivity in Medicare patients, less favourable formulary positioning or a deliberate policy not to bid for government channels. Rybelsus is relatively new and as such would not be expected to have yet achieved significant Medicare penetration.

- In a scenario where Medicare coverage were to expand to cover the 61-65 age cohort, we could see a 4.0% volume reduction in Ozempic if its share were to shift to the current share in government channels. Conversely, if Ozempic could replicate its current share in commercial channels to government channels, that would drive volumes +8.7%.

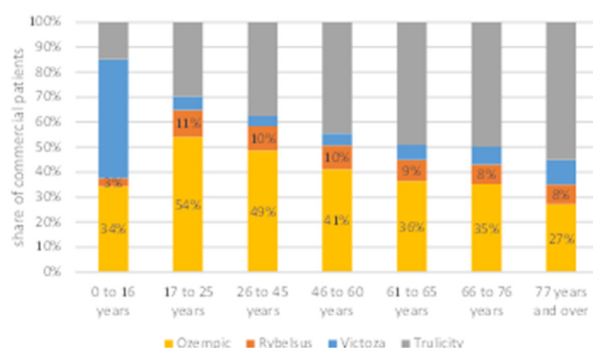**Figure 22: 2021 market share by demographics (commercial payers)**

Source: Credit Suisse Healthcare Database

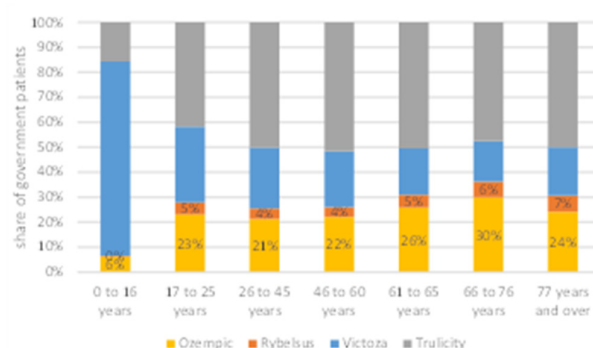**Figure 23: 2021 market share by demographics (government payers)**

Source: Credit Suisse Healthcare Database

Figure 24: 2021 GLP-1 share (commercial payers)

Source: Credit Suisse Healthcare Database

Figure 25: 2021 GLP-1 share (government payers)

Source: Credit Suisse Healthcare Database

- Our analysis of gross-to-net pricing shows higher rebates for Trulicity and Victoza vs Ozempic 2021 US rebates (see Figure 85), which could suggest higher rebating to maintain volume in government channels.

- The progression of demographics by age and by payer was relatively minor from 2018 to 2021, with increasing Medicaid patient mix from 4% to 8% being the only notable trend. However, the database gives us key insights into the shift by treatment, and GLP-1s have seen greater share gain in commercial payers, driven by Ozempic and Rybelsus. That said, GLP-1 share gain has also been strong in government-payer over-65s, driven by Trulicity adoption in this population. SGLT-2 share gain has been strongest in government payers, with DPP-4s and insulins losing market share across the board.

- We detail the age and funding demographics of the key classes of drugs in the methodology section, and overall payer split in Figure 115 to Figure 120.

**Therapeutic class transitions: the rise of GLPs and SGLT-2s**

- Sankey plot analysis allows visualisation of key trends at both the drug class and the individual drug level (full details of how to read Sankey plots is detailed on page 54).

- In 2021, we saw around 330K transitions of treatment. The weekly GLPs accounted for 195K, with DPP-4s seeing a decline of 126K, metformin use having increased by 80K, followed by SGLT-2s at +71K, -78K for the SUs and -71K for basal insulin.

- Trulicity remains ahead of Ozempic in terms of overall new transitions for all of 2021, gaining 48% of new GLP-containing treatment choices in 2021, against 38% for Ozempic. Victoza remained a choice for new GLP for 7% of patients, with Rybelsus picking up a 7% share of new GLP use. In 2020, Trulicity accounted for 54% of new transitions, Ozempic 31% and Rybelsus 3%. Absolute transitions to a GLP increased 15% from 2020 to 2021.

- This data is annual and so we need to look at it in combination with the monthly data shown in Figure 2 and Figure 4 which show the clear trend towards use of Ozempic developing through 2021.

In Figure 28, we show the transitions between drug classes in 2021 using a Sankey plot, which shows changes in uses of drug classes that occurred more than 1,000 times. Metformin (biguanide) remains the principal drug to start patients on (lilac blocks in charts) with growing use of GLP weekly treatment (pink block) and SGLT-2s (grey blocks). Sulphonyl ureas (SUs) (mid-blue blocks) and basal insulin (lime green blocks) are falling in importance but still represented substantial use in 2021.
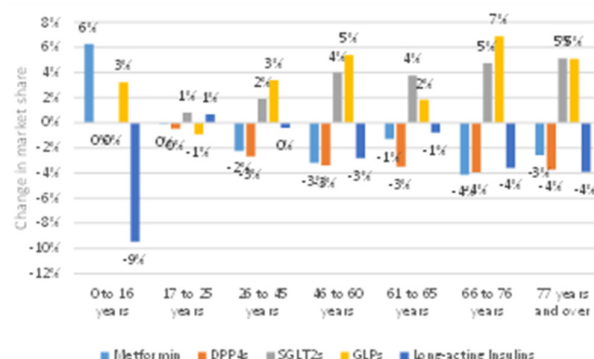
The element "added drug class" denotes a drug being added to an existing treatment/cocktail whereas a "started drug class" reflects a new entrant to the database (transferring from an alternate healthcare provider, or an initial diabetes claim). Patients are double-counted if they take more than one drug (e.g. a patient that starts on metformin and an SU will count twice). A patient must take a drug for at least six months to qualify as having made a transition. For a detailed review of how to read these charts, please turn to commentary on page 54 regarding Figure 110 to Figure 112.

Figure 26: Market-share changes in commercial channels, 2018-2021
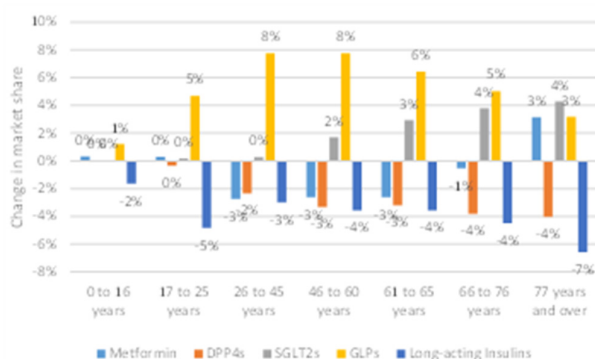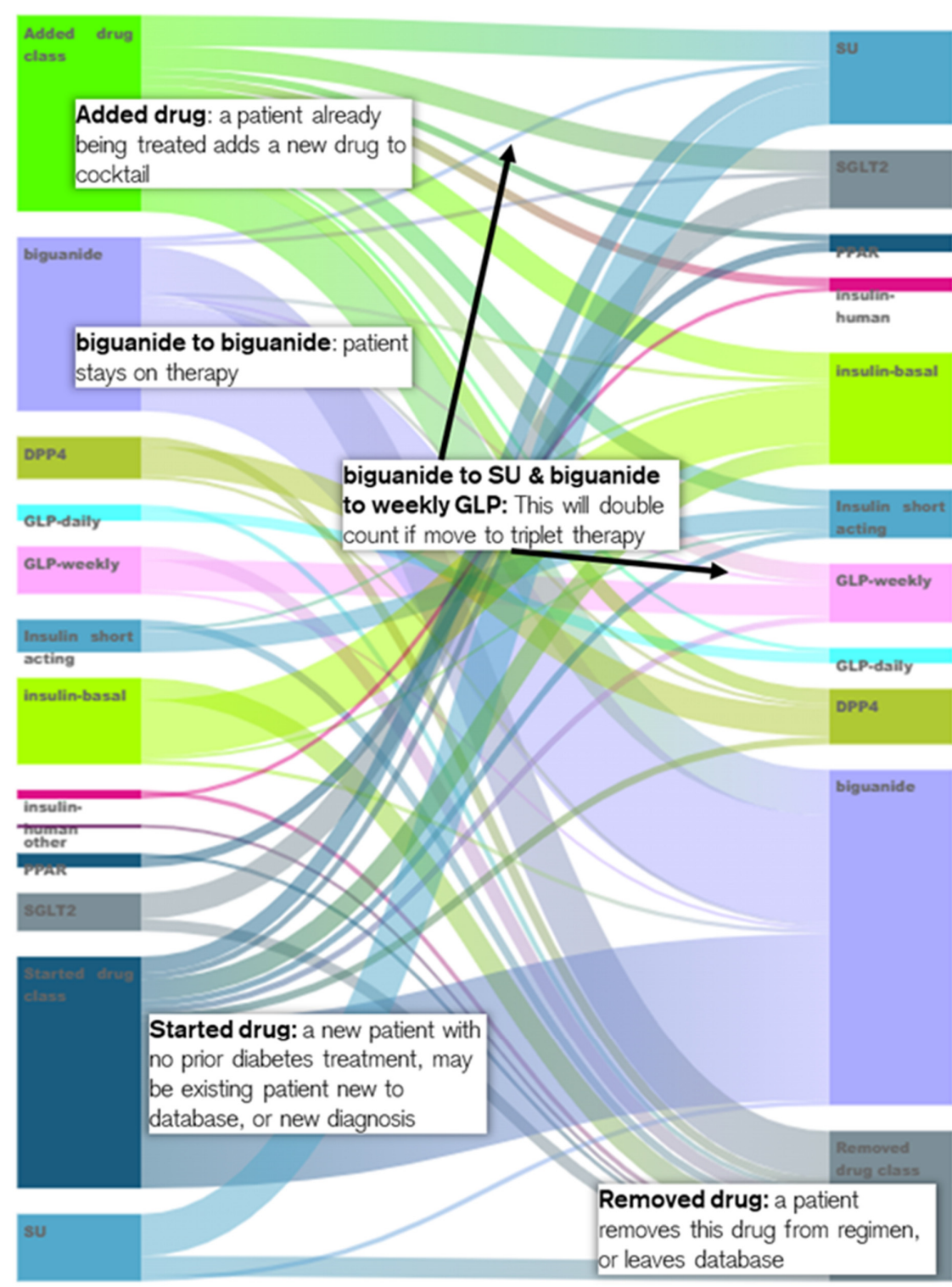

Source: Credit Suisse Healthcare Database

Figure 27: Market-share changes in government channels, 2018-2021

Source: Credit Suisse Healthcare Database

Figure 28: Drug transitions in 2021

Added drug: a patient already being treated adds a new drug to cocktail

biguanide to biguanide: patient stays on therapy

biguanide to SU & biguanide to weekly GLP: This will double count if move to triplet therapy

Started drug: a new patient with no prior diabetes treatment, may be existing patient new to database, or new diagnosis

Removed drug: a patient removes this drug from regimen, or leaves database
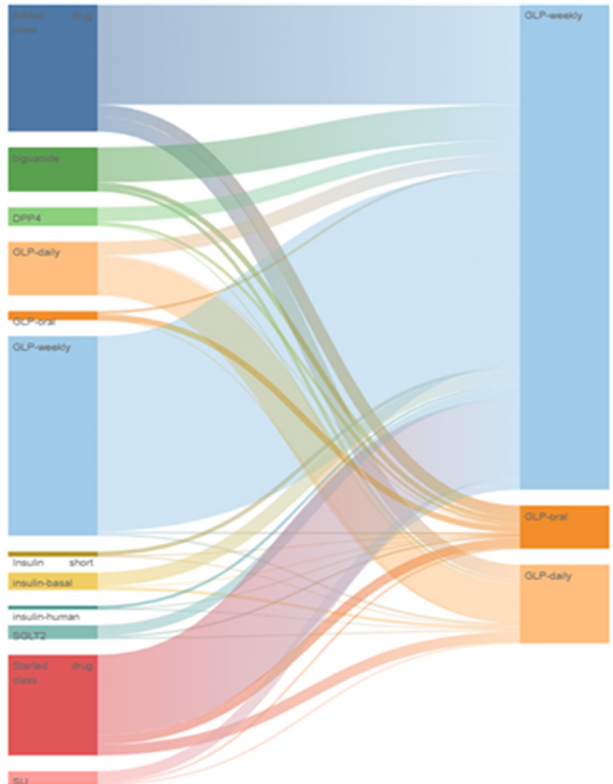
Source: Credit Suisse Healthcare Database

In the charts below, we look at the transitions into and away from the GLP class in 2021, while in Figure 31 to Figure 34 we look at the specific drug transitions within the GLP class. Of note, we see:

Moving to the GLPs: We have two main sources of new patients: 1) labelled in the Sankey plot as "added drug class", these are patients who are already on treatment and are intensifying therapy; and 2) labelled as "started class", these patients are naive to treatment in this database. For both groups of patients, we see that 80% got to a weekly treatment and 10% each moved to oral Rybelsus or daily GLP injections. In 2020, this split was 73% to weekly, 20% to daily injections and 7% to Rybelsus.

■ **Moving away from the GLPs:** Around 28% of daily injectable GLP users moved away from the class in 2021, with only 13% trading up to a weekly treatment. Less than 10% moved to insulin. We saw no material move of patients from a daily injection to a daily oral regime in this cohort of patients (we see only 500 transitions out of over 3m drug transitions).

Figure 29: Transitions by drug class to GLP class, 2021

Source: Credit Suisse Healthcare Database

**Figure 30: Transitions from GLP by drug class, 2021**
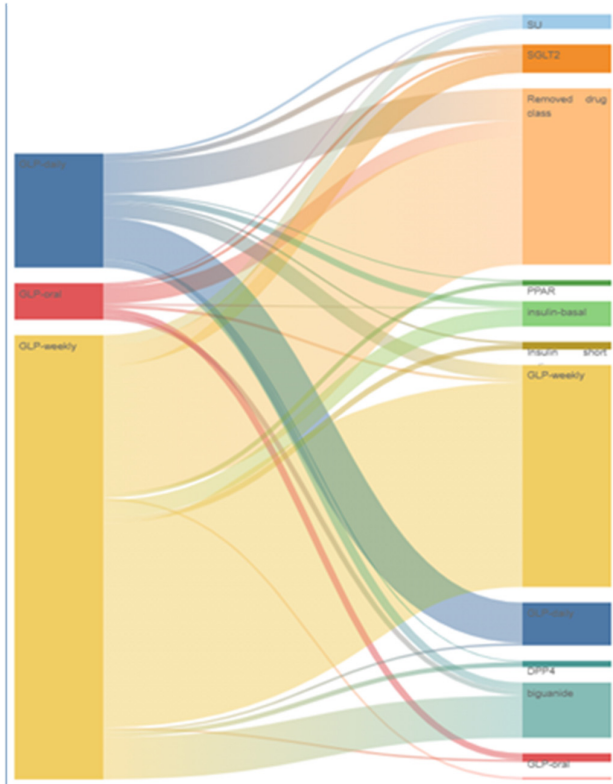
Source: Credit Suisse Healthcare Database

**Sankey plot analysis: Trulicity ahead in new GLP-1 market share in 2021**

■ In this section, we look at patient flow to the GLPs in 2021. We have simplified the Sankey plots, showing only drugs where there are at least 1,000 transitions noted in the Credit Suisse Healthcare Database. Where a patient both starts and finishes on the same drug, this reflects a full 12 months of treatment. For more information on Sankey plots, please see the section on page 54.

■ In 2021, the Credit Suisse Healthcare Database recorded c.294K switches of treatment to include GLP-1. Trulicity added 48% of new share, with Ozempic at 38%. Victoza saw 7% share, with Rybelsus picking up 7% of new GLP-1 scripts. If we look at patients who are adding a GLP-1 to existing treatment, Trulicity retains a higher share.

■ However, if we look just at patients who come in new to the database, or without prior diabetes treatment, we see that Ozempic has a higher share, with 52% of 55K additions recorded. Rybelsus accounts for 10% and Victoza still has what we view as a surprisingly high 8% of new starts. Transitions away from the GLP-1s in 2021 are shown in Figure 36. We have once again removed any transitions occurring less than 1,000 times.

■ As we show in Figure 8, leadership in new patient starts switched to Ozempic in mid-2021.

Figure 31: Transitions onto GLP-1 treatment in 2021
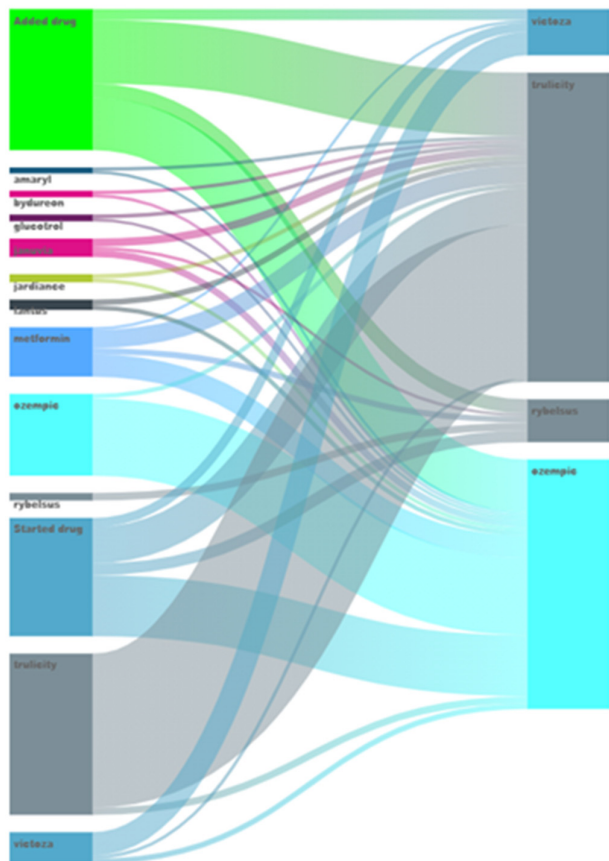
Source: Credit Suisse Healthcare Database (excludes under 1,000 transitions)

Figure 32: Transitions from GLP-1 treatment in 2021
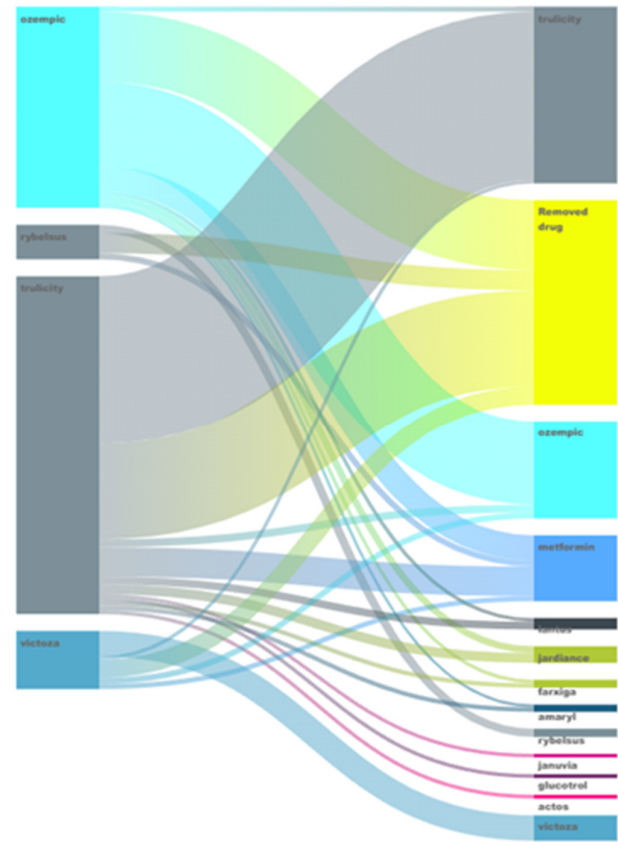
Source: Credit Suisse Healthcare Database (excludes under 1,000 transitions)

- There remains a high degree of patient churn. In 2020, we saw around 37% of starting combinations of treatment including a GLP change over the year, and this moved up to c.50% in 2021. All of this increase comes from a higher proportion of patients dropping treatment in 2021.

- We see limited switching between the various GLP-1 brands and very limited switch from injectable to oral.

- In both 2020 and 2021, we see a small preference to move to Ozempic over Trulicity from Victoza where patients moved from daily to weekly treatment. Rybelsus also gained a slightly higher number of patients from Ozempic than Trulicity, but the numbers were small.

- In 2020, we saw c.2,000 transitions from Ozempic to Trulicity but 3,800 transitions from Trulicity to Ozempic. In 2021, we saw a similar c.2,000 transitions from Ozempic to Trulicity but slightly lower transitions to Ozempic at 3,200.

Figure 33: Transitions within GLP-1 treatment in 2020

Source: Credit Suisse Healthcare Database (excluding under 100 transitions)

Figure 34: Transitions within GLP-1 treatment in 2021

Source: Credit Suisse Healthcare Database (excluding under 100 transitions)

" Two key parameters for drug modelling are patient persistence on treatment (length of overall treatment) and compliance (whether patients take the drug 100% of the time).

# Time on treatment shows high level of early abandonment

Analysis of the CS database shows around 10% abandonment after one month, 25 -30% abandonment by month four. Looking at the cohort of patients starting Trulicity in 2015 and still active in the database at the end of 2021 we see a mean persistence of close to 40 months.

- Two key parameters for drug modelling are patient persistence on treatment (length of overall treatment) and compliance (whether patients take the drug 100% of the time). An answer to both of these questions helps us understand how many patients in a real-world setting are taking a drug – and thus market penetration and the opportunity to change treatments and the likely level of dynamic market-share changes.

- Injectable treatments show a high level of abandonment at >10% after first treatment, effectively at Month 1, and 25-30% of treatments are stopped before Month 4. Novo expects the real-world mean persistence will be c.50 months for Ozempic, which it believes is in line with Trulicity. We see median patient persistence of 16 months for both. It is too early to calculate accurately the mean Ozempic persistence, but our analysis of Trulicity stay time since 2015 indicates a mean persistence closer to 40 months.

- Compliance analysis shows 80% of expected claims made for metformin, an average of 70% for insulins, with slightly higher compliance for Trulicity (74%) than Ozempic (71%). On a limited sample, Rybelsus compliance is high (82%), only slightly behind Farxiga (84%).

**Time on treatment only around two years for all drug classes**

- A key benefit of the Credit Suisse Healthcare Database is that it allows us to look longitudinally at cohorts of patients to better understand stay time on medications. We have looked at this to see whether there is any one class that shows longer stay time and therefore more apparent patient/doctor satisfaction with treatment, and to review a long-standing debate in the GLP-1 class over persistence on therapy.

- In this analysis, there is little difference between Trulicity and Ozempic in terms of persistence of treatment starting either at launch or at four months post, with the erosion lines overlaying each other. The initial Rybelsus data for 2019 is limited, so we present 2020 with a larger cohort.

- In Figure 41, we show the time on treatment for each of the key classes of drug.

- In the methodology section and in our individual drug profiles, we show stay times for patients starting treatment in 2017 or if launched later as early as possible to capture as full a data set as possible. Our analysis reveals a very high level of drug abandonment between Months 1 and 3. We have therefore reviewed persistence based on both time from first treatment and from Month 4 onwards.

Figure 35: Persistence of GLP treatment 2019 cohort (from first treatment and Rybelsus also from 2020)
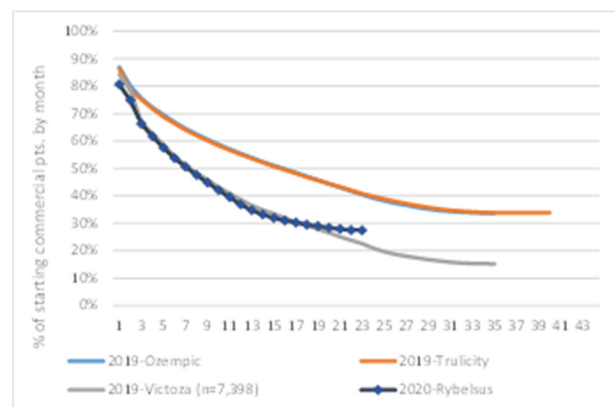
Source: Credit Suisse Healthcare Database, Credit Suisse

Figure 36: Persistence of GLP treatment from four months, 2019 cohort (from first treatment and Rybelsus also from 2020)
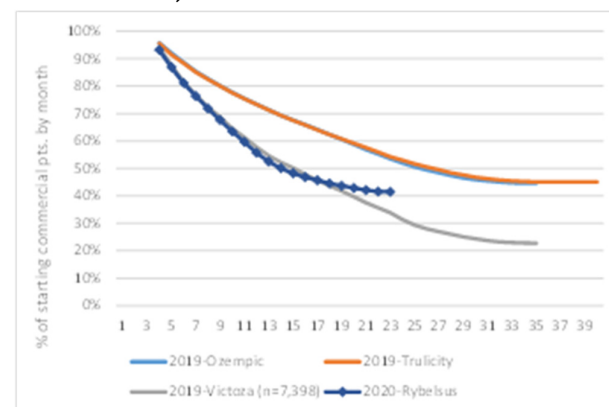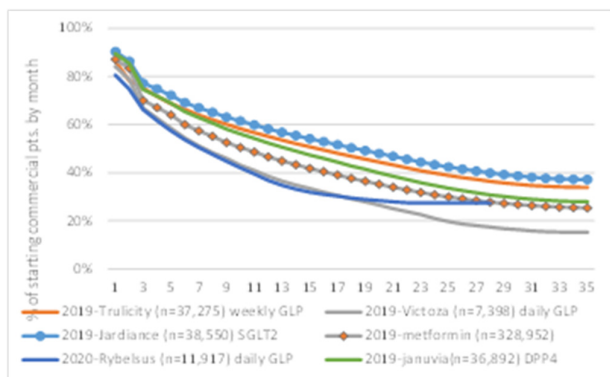

Source: Credit Suisse Healthcare Database, Credit Suisse

- We have restricted our analysis to the subsegment of patients in the database who remain enrolled in the database today, to eliminate any artificial treatment loss due to patient churn.

- The stay time for metformin recorded in the Credit Suisse Healthcare Database is surprisingly short as this is a foundational therapy. We assume that this may reflect periodic stopping of metformin as treatment is intensified before starting once again and being counted here as a new starter.

Rybelsus persistence in 2020 looks lower than either weekly GLP-1 Trulicity or Ozempic. We assume this reflects the fact that Rybelsus is much earlier in its launch (US launch end of 2019) vs Ozempic (2018) and Trulicity (2014) and thus a greater proportion of patients are simply new to starting the drug. We need more data to establish if more drop-outs/a shorter stay time on the drug is inherently more common on Rybelsus.

Figure 37: 2019 time on treatment: different classes from first launch

Source: Credit Suisse Healthcare Database, Credit Suisse

Figure 38: Erosion rates over time show great consistency
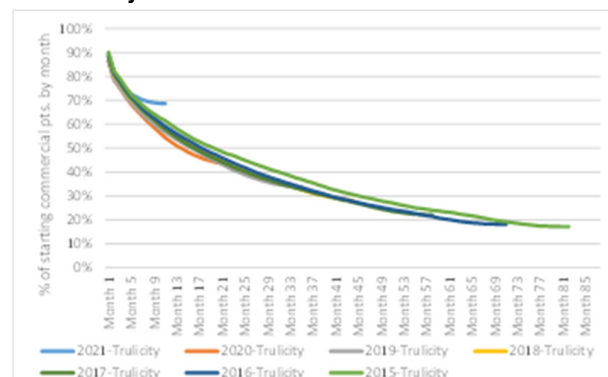
Source: Credit Suisse Healthcare Database, Credit Suisse

Figure 39: Months of treatment to reach 50% drop-off (median patient persistence) based on various-year cohorts and either starting from initial treatment or counting only from Month 4 when prescriptions are established

From	class	2017		2019		2020	
		Start	Mth 4	Start	Mth 4	Start	Mth 4
metformin	oral biguanide	15	27	9	20	8	17
Trulicity	Weekly GLP inj.	16	27	16	27	13	58% at 23 mths
Ozempic	Weekly GLP inj.			16	27	13	55% at 23 mths
Farxiga	oral SGLT2	18	27	16	25	14	57% at 23 mths
Invokana	oral SGLT2	12	22	16	24	12	53% at 23 mths
Jardiance	oral SGLT2	23	35	18	30	15	60% at 23 mths
Victoza	Daily GLP inj.	11	15	8	15	8	15
Rybelsus	oral GLP					7	15

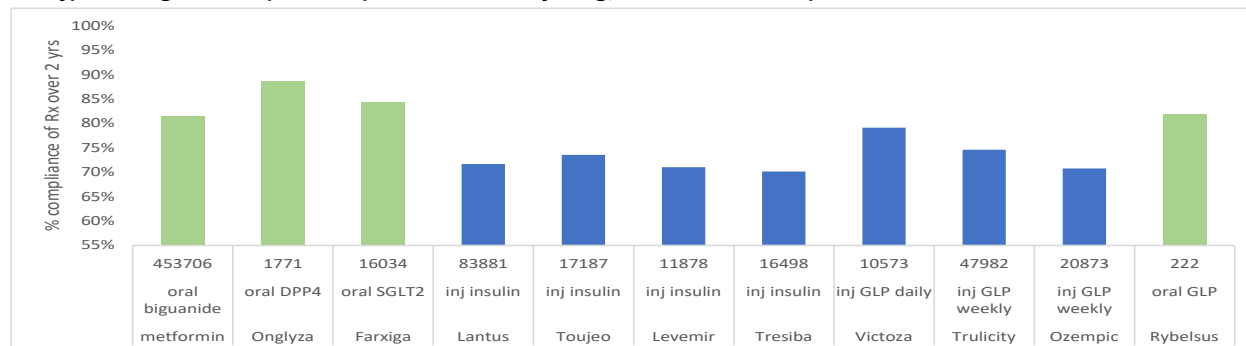Source: Credit Suisse Healthcare Database, Credit Suisse

Patient compliance typically 70-80% to full treatment

The Credit Suisse Healthcare Database is based on Rx (prescription) and Mx (medical) claims. Although it cannot speak to the direct consumption of pharmaceuticals, we can look at the number of claims made between the start and the end of treatment and for any breaks in treatment that indicate the actual level of compliance. In Figure 40, we look at the number of claims made over a two-year period for subscribers who were taking a specific drug at both the start and the end of this period (2019-21). We have then looked at the theoretical number of claims we would have expected – given the typical length of a script – and note the percentage of actual claims made versus the theoretical number of claims made for full compliance that we can see in the database. We also show the number of subscribers in each sample (note that Rybelsus' sample size is low given launch only in 2019). This data set is important for modelling longer-term sales as it suggests that in most cases patients do not claim for a full 12 months of treatment even when settled on a chronic treatment for an extended period of time, that should be used regularly, in the case of diabetes either daily or weekly.

We note generally higher compliance for orals over injectables; this includes apparently strong compliance for Rybelsus despite the known requirement to fast for 30 minutes post dosage. We note the apparently higher compliance for Trulicity over Ozempic, with >20,000 patients counted for both.

Figure 40: Compliance with drug treatment for selected drugs based on % claims made out of expected level given the typical length of scripts. Sample size shown by drug; orals shown in separate colour

Source: Credit Suisse Healthcare Database

"For each drug, we provide a Credit Suisse Healthcare Database profile.

Credit Suisse Healthcare Database: Product profiles

For key diabetes drugs we profile time on treatment, transitions between drugs, copays and overall source of funding for patients.

Ozempic (Novo Nordisk)

Ozempic is a weekly injectable GLP-1 manufactured by Novo Nordisk. The drug was launched in the US in 2018, and in 2021 recorded sales of $3.7bn in the US ($5.4bn worldwide). We model a $7bn peak sales opportunity in the US ($12.5bn peak worldwide).

Time on therapy

Looking at time on therapy, we see a 14% drop-out rate after one month. If we count sustained treatment as starting only from Month 4, we see a 50% drop-off by c.26 months in the longest cohort we have data for, which is for patients starting treatment in 2018, and who were still active subscribers to the database in 2021. This is a substantially shorter period than the c.50 months reported by Novo. This data must have been based on an extrapolation of trends data, given that Ozempic had been launched at that time for only c.45 months.
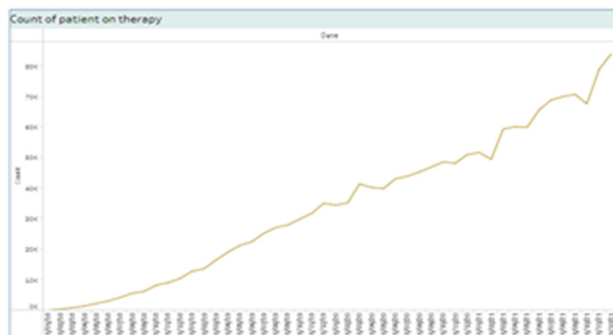
Co-pays

Ozempic median co-pays by channel have declined over the past three years and are below GLP-1 average co-pays.
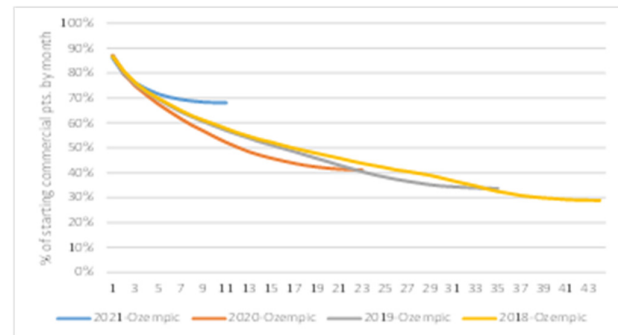
Funding channel

We see Ozempic as under-prescribed in the 66-76 years and 77+ years categories. 78% of Ozempic prescriptions in this data set are for commercial patients (down from 85% in 2020).

Figure 41: Credit Suisse Healthcare Database count of patients on Ozempic, 2018-2021

Source: Credit Suisse Healthcare Database

Figure 42: Time on therapy: Ozempic patients, erosion from start of treatment
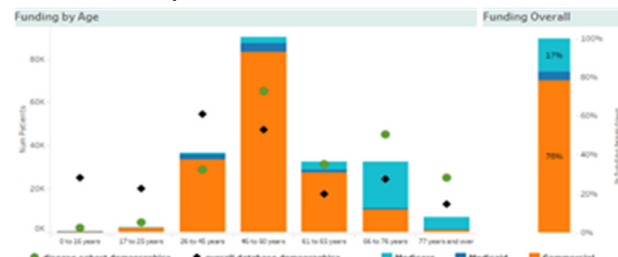

Source: Credit Suisse Healthcare Database

Figure 43: Ozempic median co-pay by channel, 2018-2021

Source: Credit Suisse Healthcare Database

Figure 44: Funding by age and overall funding, 2021 for Ozempic
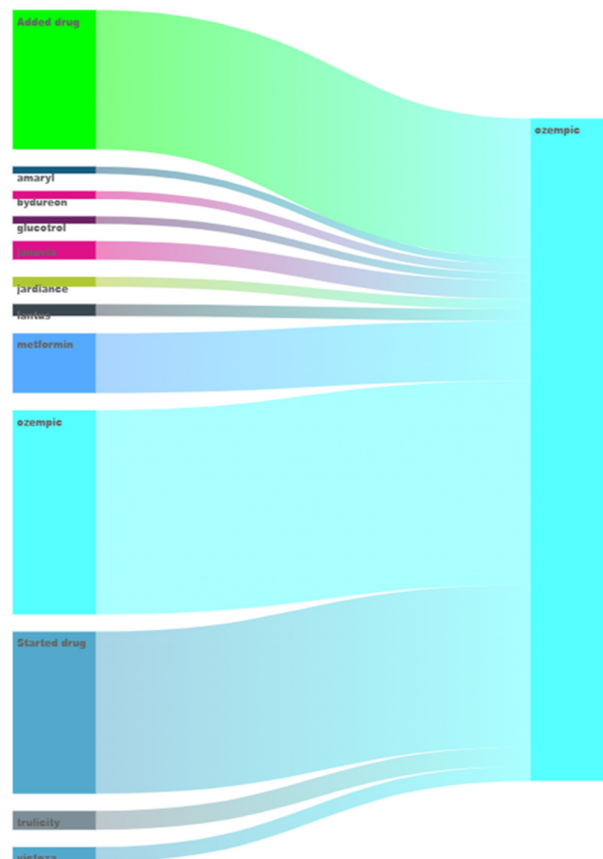

Source: Credit Suisse Healthcare Database

Patient flow

The patient flow into Ozempic in 2021 came from a wide range of prior therapies. Of patients who switched to or added Ozempic within 2021, c.25% started Ozempic without prior therapy within this database and c.21% of patients added Ozempic to an existing regimen. For straight switches, c.2% of patients came from Victoza, c.9% from metformin, c.3% from Trulicity and <1% from Rybelsus.

When we look at patient flows away from Ozempic in 2021, we see c.42% of patients that completed six months of treatment remaining on therapy for a full 12 months. The rest of the patients changed therapy: c.3% of patients moved to the competitor injectable Trulicity and c.1% of patients moved to the oral GLP-1 therapy Rybelsus.

Figure 45: 2021 patient flows to Ozempic

Source: Credit Suisse Healthcare Database (excludes under 1,000 transitions)

Figure 46: 2021 patient flows from Ozempic
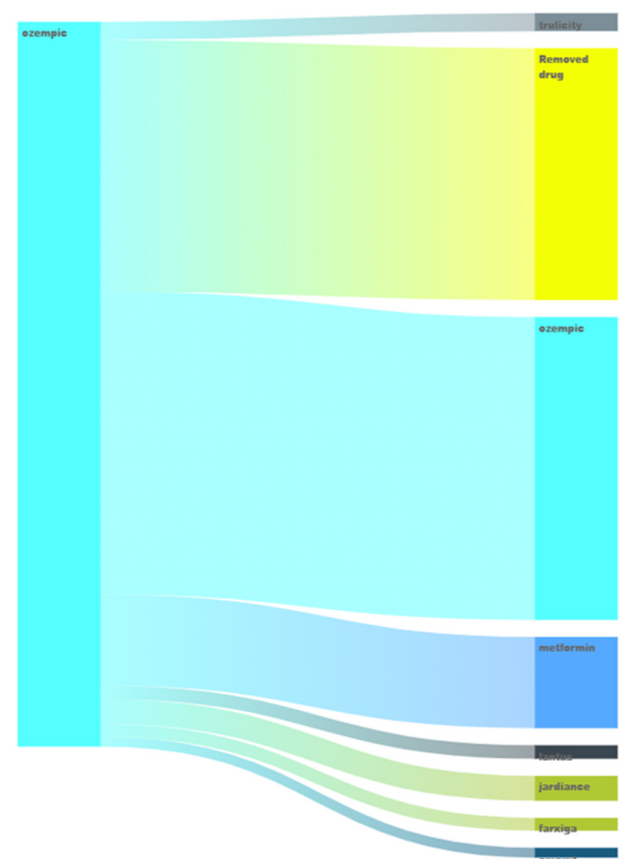
Source: Credit Suisse Healthcare Database (excludes under 1,000 transitions)

Trulicity (Eli Lilly)

Trulicity is a weekly injectable GLP-1 manufactured by Eli Lilly. The drug was launched in the US in 2014, and in 2021 recorded sales of $4.9bn in the country ($6.5bn worldwide). Evaluate consensus forecasts a $7.4bn peak sales opportunity worldwide before patent expiry in October 2028.

Time on therapy

Looking at time on therapy, we see a very similar erosion curve for each of the annual cohorts of treatment. We see a 12% drop-out rate after one month. If we count from first dose, we see a 50% drop-off by Month 16, but if we count sustained treatment as only from Month 4, we see a 50% drop-off at Month 27. This is very similar to Ozempic.
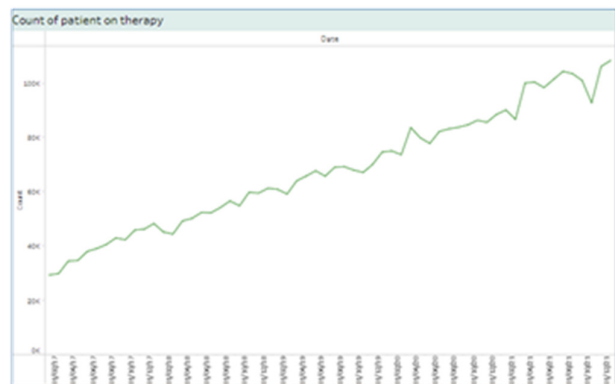
Co-pays

Trulicity median co-pays by channel have declined slowly over the past three years. Medicaid co-pays were <$3 in 2021. This compares with c.$6 for Ozempic in the same channel.
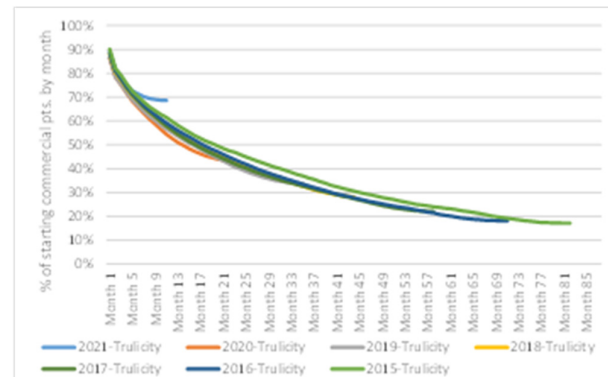
Funding channel

We see Trulicity as under-prescribed in the 26-45 years, 66-76 years and 77+ years categories. Of Trulicity prescriptions in this data set, 68% are for commercial patients.

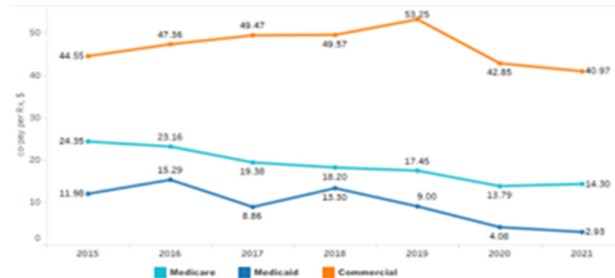**Figure 47: Count of patients on Trulicity, 2017-2021**

Source: Credit Suisse Healthcare Database

Figure 48: Time on therapy for Trulicity, erosion from start of treatment, 2015-2021 cohorts
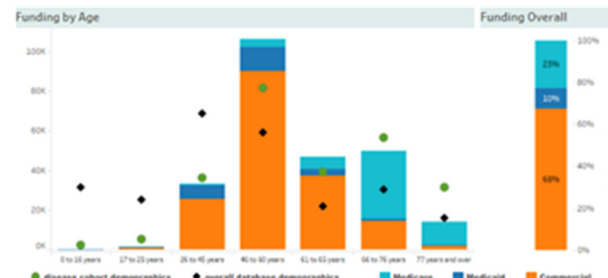

Source: Credit Suisse Healthcare Database

Figure 49: Trulicity median co-pay by channel, 2015-2021

Source: Credit Suisse Healthcare Database

**Figure 50: Funding by age and overall funding, 2021 for Trulicity**

Source: Credit Suisse Healthcare Database

Patient flow

On patient flow into Trulicity in 2021, there is a wide range of prior therapies. In this data set, of the c.140K patients in the Credit Suisse Healthcare Database who either switched to or added Trulicity in 2021 for at least six months, c.12% started Trulicity and c.21% of patients added Trulicity to an existing regimen. For straight switches from other GLPs, we see a very small but equal number of patients coming from Victoza and Ozempic (<1% of patients).

When we look at patient flows away from Trulicity in 2021, we see c.50% of patients that completed six months of treatment remaining on therapy for a full 12 months. We see c.28% removing the drug either completely or from an existing cocktail. Around 2% of patients moved to Ozempic and <1% moved to Rybelsus.

Figure 51: 2021 patient flows to Trulicity
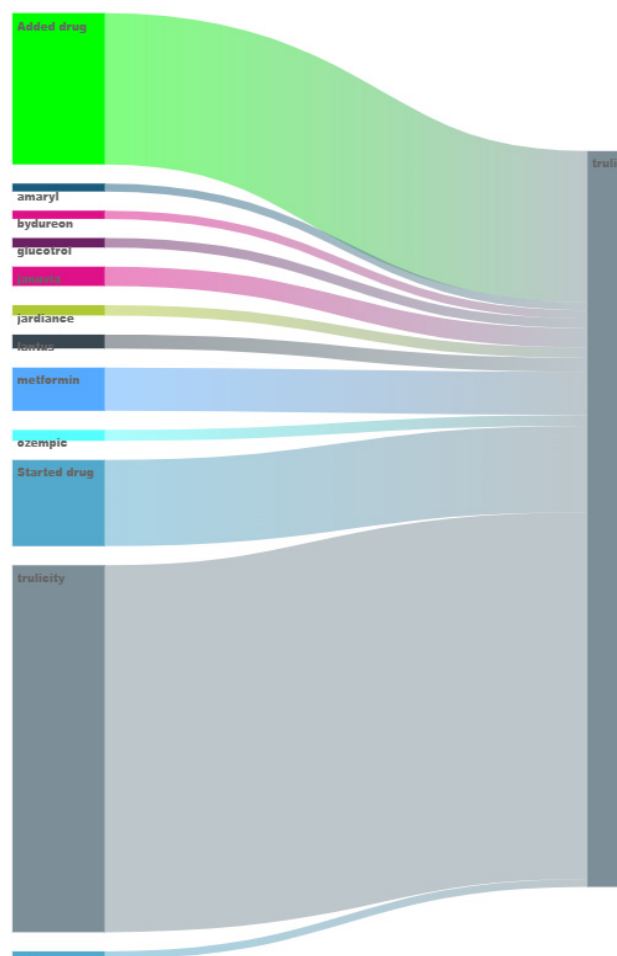
Source: Credit Suisse Healthcare Database (ignoring under 1,000 transitions)

Figure 52: 2021 patient flows from Trulicity
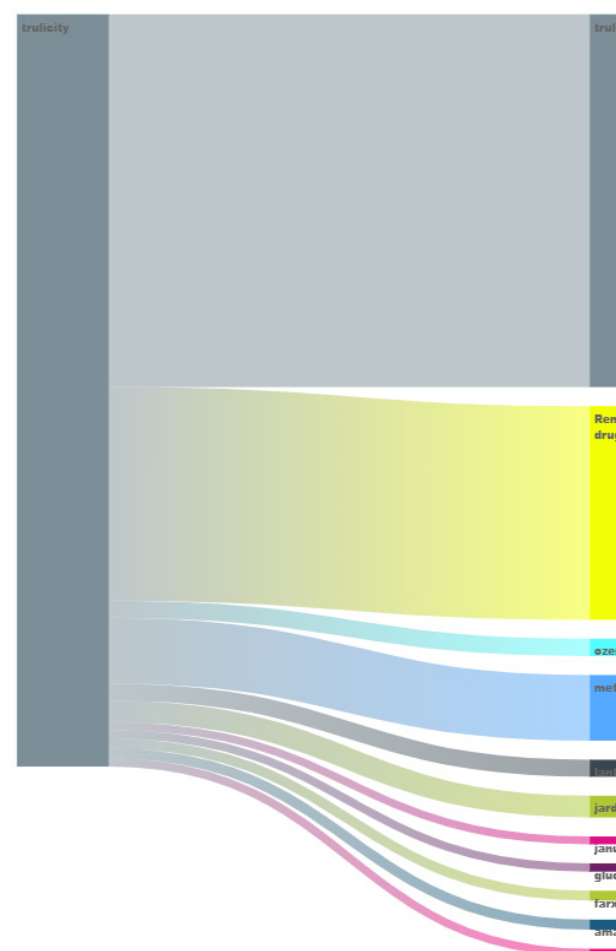
Source: Credit Suisse Healthcare Database (ignoring under 1,000 transitions)

Rybelsus (Novo Nordisk)

Rybelsus is a daily oral GLP-1 manufactured by Novo Nordisk. The drug was launched in the US at the end of 2019, recording 2021 sales of $675m in the country ($769m worldwide). We forecast a $6.5bn peak sales opportunity worldwide in diabetes only.

We note the apparent drop in Rybelsus patients in December 2021; we do not see any supporting evidence in terms of lower IQVIA TRx data and are continuing to investigate this data.

Looking at time on therapy, the 2019 cohort is for only 3,816 patients and although it shows an extremely high persistence, this is not followed by subsequent bigger cohorts. The 2020 cohort (11,917 patients) appears to follow a slightly higher erosion curve than the weekly GLP curve.
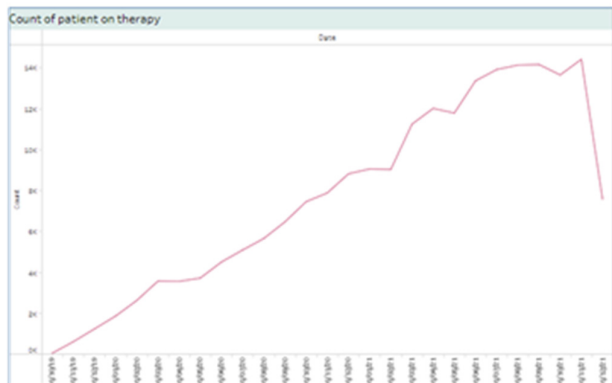
Co-pays

Rybelsus median co-pays by channel have been declining since launch in 2019. Medicaid co-pays were $5.70 in 2021, similar to the c.$6 for Ozempic. Commercial co-pays were c.$48 vs $42 for Ozempic.
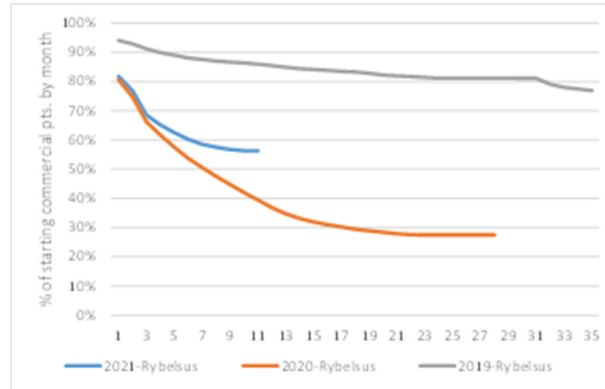
Funding channel

We see Rybelsus as under-prescribed in the over-65 categories. The older patients will likely require more Medicare coverage/penetration. The penetration in the 26-45 age range being at a par with other diabetes drugs suggests that Novo is correct in seeing Rybelsus as increasingly used as an intensification to metformin.

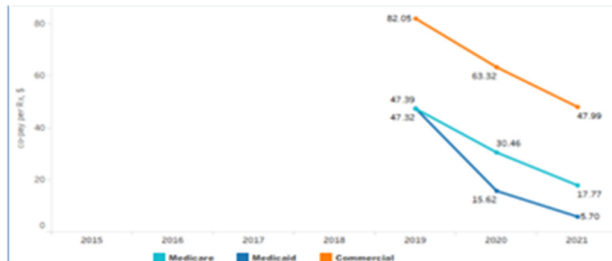**Figure 53: Count of patients on Rybelsus, 2019-2021**

Source: Credit Suisse Healthcare Database

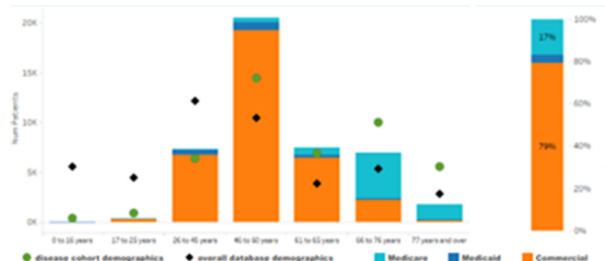**Figure 54: Time on therapy for Rybelsus, erosion from start of treatment**

Source: Credit Suisse Healthcare Database

Figure 55: Rybelsus median co-pay by channel, 2019-2021

Source: Credit Suisse Healthcare Database

**Figure 56: Funding by age and overall funding, 2021 for Rybelsus**

Source: Credit Suisse Healthcare Database

Patient flow

On patient flow into Rybelsus in 2021, there is a wide range of prior therapies. We saw around 22% of patients starting the drug as a sole agent, with 27% adding the drug to an existing cocktail. We see a small but equal move from the injectable Trulicity and Ozempic (each around 2.5%). Around 12% of patients moved from metformin.

When we look at patient flows away from Rybelsus, we see that about 18% of patients who had completed six months of treatment remained on therapy for a full 12 months. We see a move back to metformin (or a combination with metformin) for c.14% of patients. Interestingly, we see little move from Rybelsus to the injectable GLP-1s in this data set, although where there is transition it seems to slightly favour Ozempic (c.5%) vs Trulicity (c.2%).

Figure 57: 2021 patient flows to Rybelsus
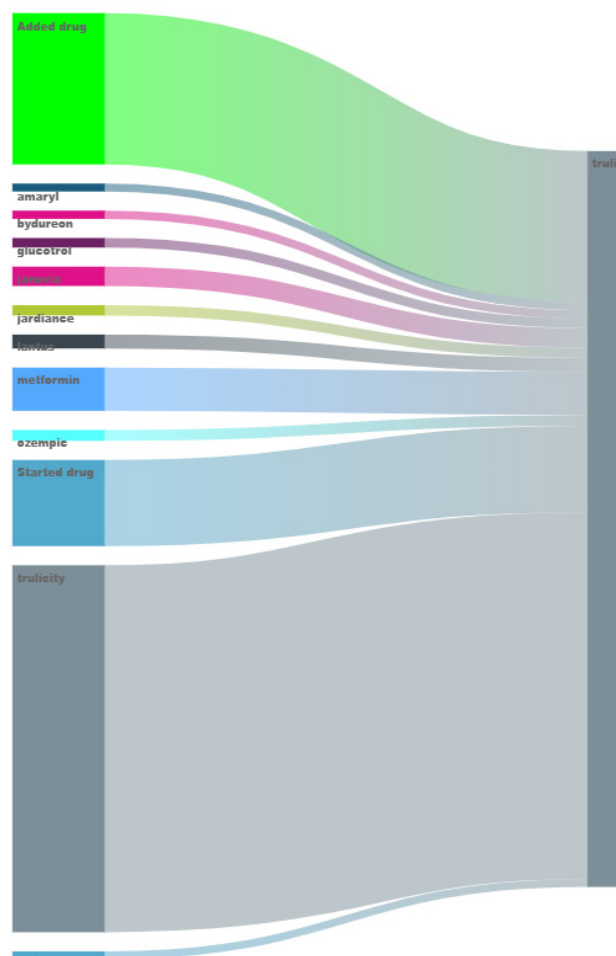
Source: Credit Suisse Healthcare Database (ignoring under 100 transitions)

Figure 58: 2021 patient flows from Rybelsus
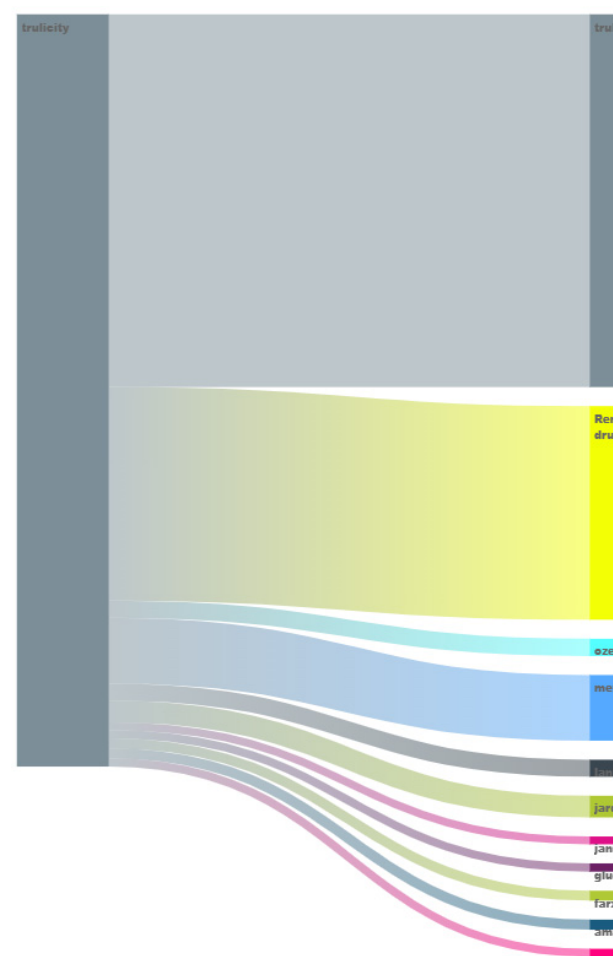
Source: Credit Suisse Healthcare Database (ignoring under 100 transitions)

Victoza (Novo Nordisk)

Victoza is a daily injectable GLP-1 manufactured by Novo Nordisk. The drug was launched in the US at the end of 2010. It recorded sales of $1.3bn in the US ($2.4bn worldwide). We assume Victoza has already passed its peak sales year, given the advent of weekly GLP-1 alternatives. Victoza's US patent will expire in mid-2024.

Looking at time on therapy, there is a similar level of abandonment after one script (c.14% of all 2020 initiations for Victoza ended after one script versus 14% for Ozempic and for Trulicity). The overall erosion curve remains higher for Victoza than for other GLPs, with a 50% erosion from first treatment at around 11 months for the 2017 cohort falling to eight months in later cohorts. If we look only at those patients who have persisted for four months, we still see 50% erosion at 15 months. This compares with c.38 months quoted by Novo for Victoza.
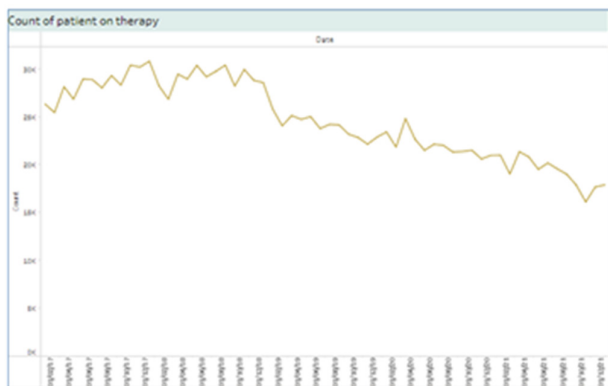
Co-pays

Victoza median co-pays have declined slowly over the past three years for Medicaid and Medicare, to c.$14 and c.$2, respectively. Conversely, commercial co-pays have increased to c.$47.
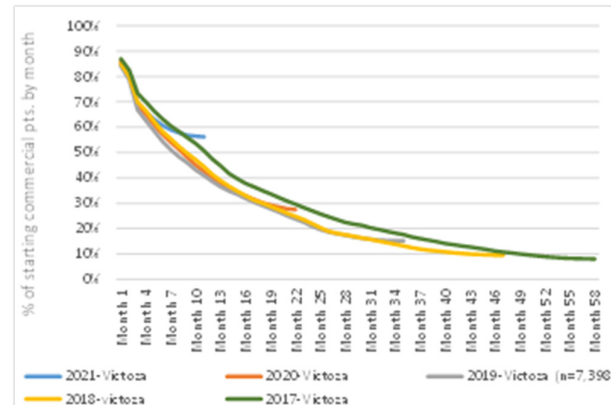
Funding channel

Of Victoza prescriptions in this data set, 39% are for commercial patients, a much lower proportion than for other GLPs (79% for Rybelsus, 78% for Ozempic and 68% for Trulicity).

Figure 59: Count of patients on Victoza, 2017-2021
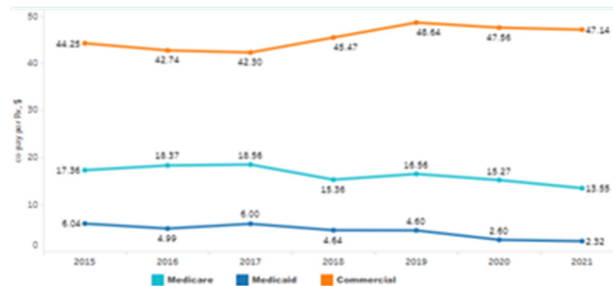

Source: Credit Suisse Healthcare Database

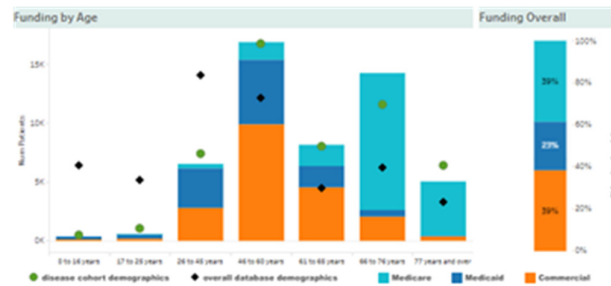**Figure 60: Time on therapy for Victoza, erosion from start of treatment**

Source: Credit Suisse Healthcare Database

Figure 61: Victoza median co-pay by channel, 2015-2021

Source: Credit Suisse Healthcare Database

**Figure 62: Funding by age and overall funding, 2021 for Victoza**

Source: Credit Suisse Healthcare Database

Patient flow

On patient flow into Victoza in 2021, there is a wide range of prior therapies. In this data set, of the patients who either switched to or added Victoza in 2021, c.17% started Victoza without prior therapy and 20% of patients added Victoza to an existing regimen. For straight switches, 5% of patients came from metformin; 43% of patients transitioned to stay on Victoza in 2021 (i.e., they were taking Victoza for at least six months from 2020 into 2021).

When we look at patient flows away from Victoza in 2021, we see c.36% of patients that completed six months of treatment remaining on therapy for a full 12 months. Of the patients that changed therapy, c.5% moved to only weekly Trulicity and c.9% moved to Ozempic and <1% moved to Rybelsus.

Figure 63: 2021 patient flows to Victoza
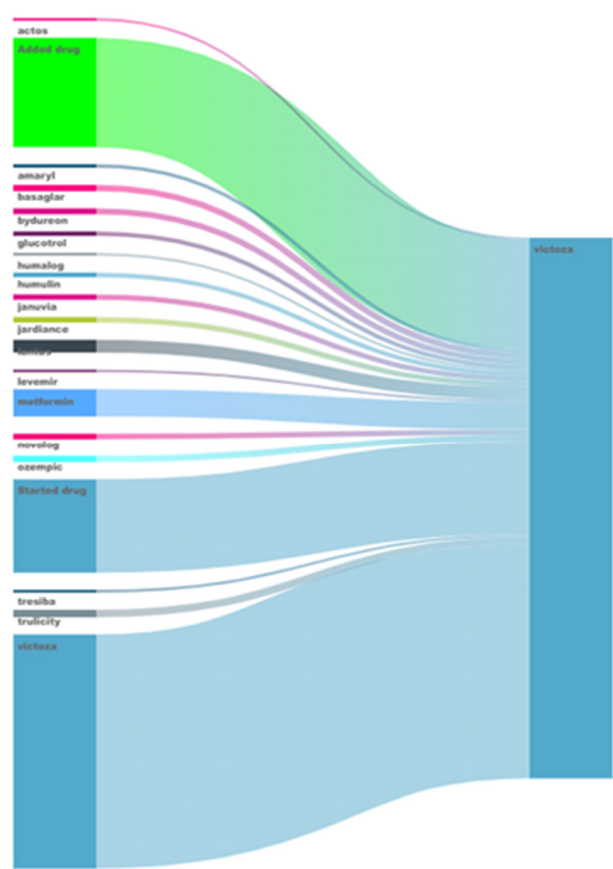
Source: Credit Suisse Healthcare Database (ignoring under 500 transitions)

Figure 64: 2021 patient flows from Victoza
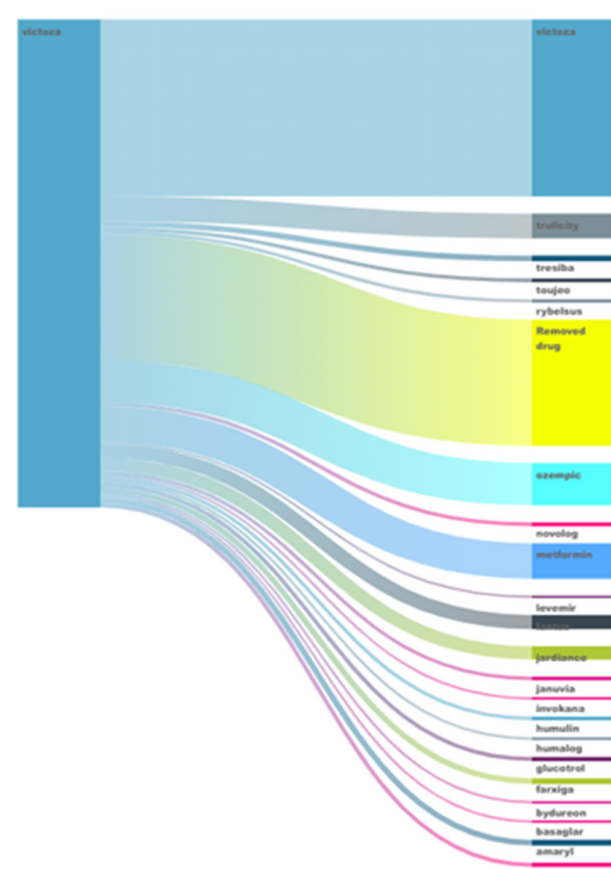
Source: Credit Suisse Healthcare Database (ignoring under 500 transitions)

Farxiga (AstraZeneca)

Farxiga is a daily oral SGLT-2 manufactured by AstraZeneca. The drug was launched in the US in 2014, and recorded 2020 sales of $732m in the country ($3.0bn worldwide), we believe largely still in diabetes. CS forecasts a $3.7bn peak sales opportunity worldwide in diabetes only (and $6.7bn overall potential peak including heart failure and chronic kidney disease). The drug loses US patent protection in April 2026. AZN is looking to combine Farxiga with other mechanisms of action to sustain the franchise beyond initial patent loss.

Time on therapy

Erosion for the class is broadly in line with other diabetes treatments, although this data set does show a measurable difference in persistence favouring Jardiance – which had early heart failure data over Farxiga and Invokana.

Co-pays

Farxiga median co-pays by channel have been declining over the past three years. This follows a similar trend for Jardiance and reflects the highly competitive nature of this category. Invokana had marginally the highest reported commercial co-pay in the class at $40 in 2021, a small rise over 2020 when both Jardiance and Farxiga saw a decline in co-pay.

Funding channel

Farxiga has 70% commercial payer funding, well ahead of other SGLT-2s. The whole category has seen a shift in funding away from commercial in recent years. Farxiga moved from 85% to 75% commercial funding between 2017 and 2020 with much higher utilisation of the drug in the elderly.

Figure 65: Count of patients on Farxiga and other leading SGLT-2s, 2017-2021
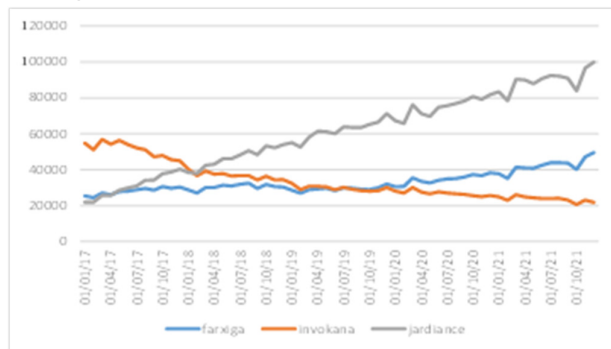
Source: Credit Suisse Healthcare Database

Figure 66: Time on therapy for Farxiga, erosion from start of treatment vs other SGLT-2s for 2017 and 2019 cohorts
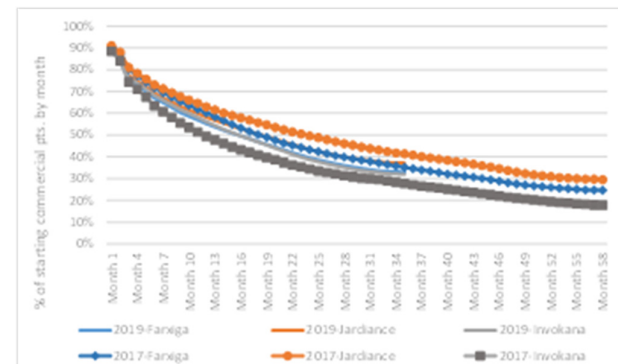
Source: Credit Suisse Healthcare Database

Figure 67: Farxiga median co-pay by channel, 2015-2021

Source: Credit Suisse Healthcare Database

Figure 68: Funding by age and overall funding, 2021 for Farxiga

Source: Credit Suisse Healthcare Database

Patient flow

Of patients that were on Farxiga in 2021, c.27% added Farxiga in combination with other therapies and c.20% started the drug (without prior record of another diabetes medication in this database). For straight switches, c.10% of patients came from metformin, c.3% from competitor SGLT-2 Jardiance and <2% from Invokana. Around 2% switched from all GLP-1s.
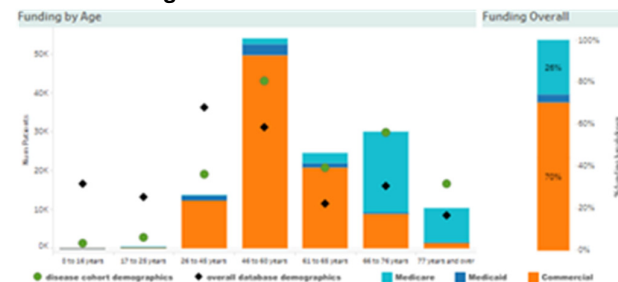
When we look at patient flows away from Farxiga in 2020, we see c.38% of patients that completed six months of treatment remaining on therapy for a full 12 months. The rest of the patients changed therapy: <5% moved to GLP-1 therapies, c.5% moved to other SGLT-2 therapies, c.9% moved to metformin and c.35% removed the drug from their regimen.

Figure 69: 2021 patient flows to Farxiga

Source: Credit Suisse Healthcare Database (ignoring under 500 transitions)

Figure 70: 2021 patient flows from Farxiga

Source: Credit Suisse Healthcare Database (ignoring under 500 transitions)

Jardiance (Boehringer Ingelheim/Eli Lilly)

Jardiance is a daily oral SGLT-2 manufactured by BI/Lilly. The drug launched in the US in 2014 and 2020 sales were $1.7bn in the country ($3.3bn worldwide). Evaluate pharma consensus is for c.$6bn peak sales worldwide.

Time on therapy

Figure 66 highlights the relative persistence for the three main SGLT-2s and Figure 72 details the data for various Jardiance cohorts. Jardiance has the best persistence of any of the SGLT-2s.

Co-pays

Jardiance median co-pays by channel have declined slowly over the past three years and are below the SGLT-2 average.

Funding channel

Jardiance funding is dominated by commercial plans, and it is relatively underused in the elderly.

Figure 71: Count of patients on Jardiance, 2017-2021
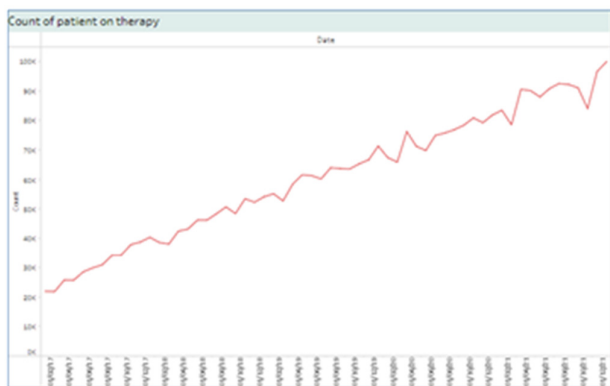
Source: Credit Suisse Healthcare Database

Figure 72: Time on therapy for Jardiance, erosion from start of treatment
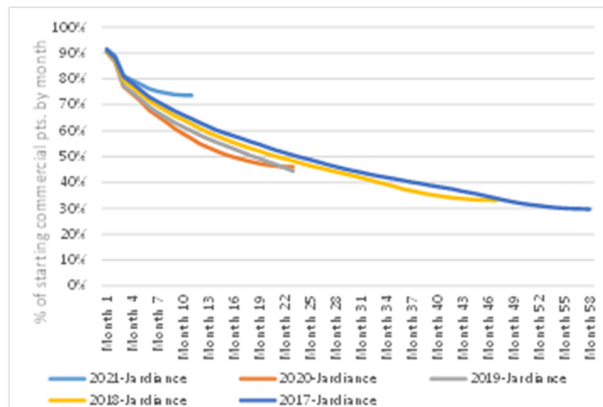
Source: Credit Suisse Healthcare Database

Figure 73: Jardiance median co-pay by channel, 2015-2021
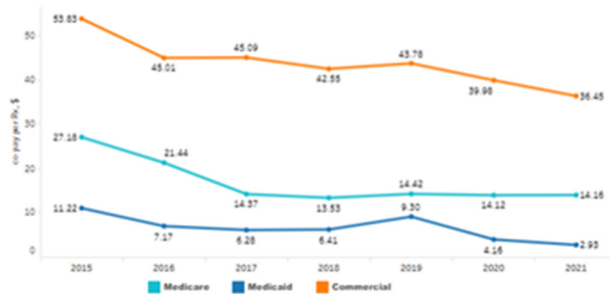
Source: Credit Suisse Healthcare Database

Figure 74: Funding by age and overall funding, 2021 for Jardiance
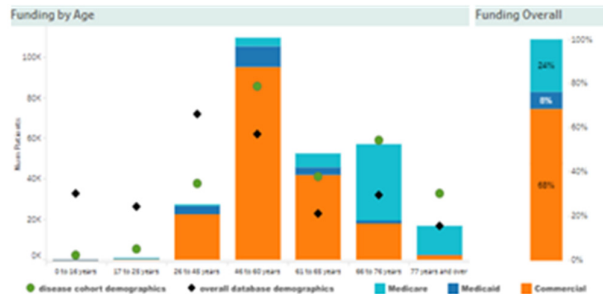
Source: Credit Suisse Healthcare Database

Patient flow

On patient flow into Jardiance in 2021, there is a wide range of prior therapies. In this data set, of the patients who either switched to or added Jardiance in 2021, c.13% started without prior therapy and 30% added Jardiance to an existing regimen. For straight switches, c.7% of patients came from metformin, c.9% from metformin, c.3% from Januvia and <2% from Farxiga.

When we look at patient flows away from Jardiance in 2021, we see c.40% of patients that completed six months of treatment remaining on therapy for a full 12 months. The rest of the patients changed therapy: c.5% moved to GLP-1 therapies, c.3% moved to other SGLT-2 therapies, c.9% moved to metformin and c.35% discontinued treatment with Jardiance.

Figure 75: 2021 patient flows to Jardiance
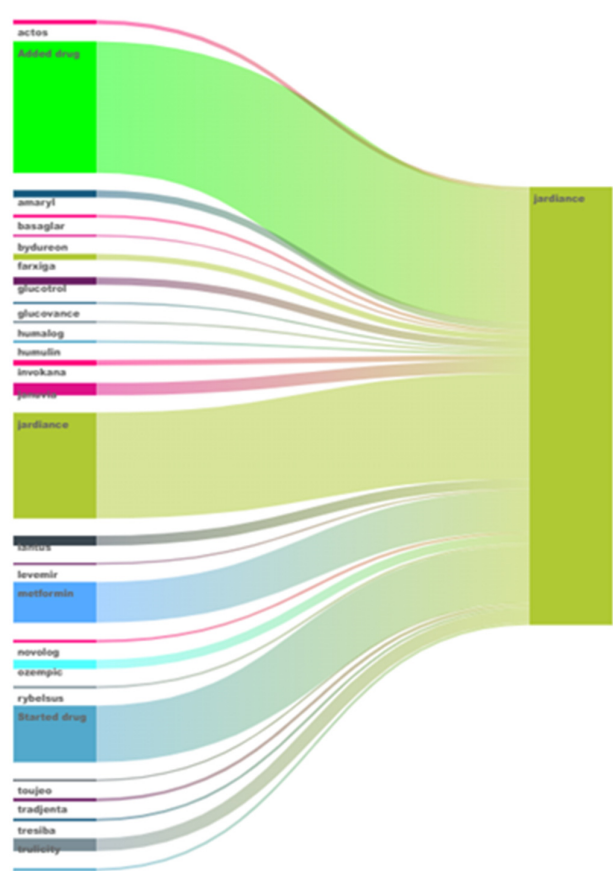
Source: Credit Suisse Healthcare Database (ignoring under 500 transitions)

Figure 76: 2021 patient flows from Jardiance

Source: Credit Suisse Healthcare Database (ignoring under 500 transitions)

Invokana (Johnson & Johnson)

Invokana is a daily oral SGLT-2 manufactured by Jansen (J&J). The drug was launched in the US in 2013 and reached peak worldwide sales of $1,438m in 2016. Sales in 2021 were $307m in the US ($563m WW), and we expect sales of $327m in the US in 2025.

Time on therapy

Figure 66 highlights the relative persistence for the three main SGLT-2s and Figure 79 shows the data for various Invokana cohorts. In this data set, Invokana has the shortest persistence of any of the SGLT-2s (see Figure 39).

Co-pays

Invokana median co-pays by channel have seen a slight decline since 2019. However, this is one of the few branded diabetes drugs to see an apparent YoY commercial co-pay increase from 2\020 to 2021. With declining patient numbers, we would assume JNJ would look to maximise revenues from existing patients.

Funding channel

Invokana has a higher mix of funding from commercial payers, although lower than other SGLT-2s. Invokana has notably higher use in elderly Medicare patients. 58% of patients were commercial in 2021.

Figure 77: Count of patients on Invokana, 2017-2021
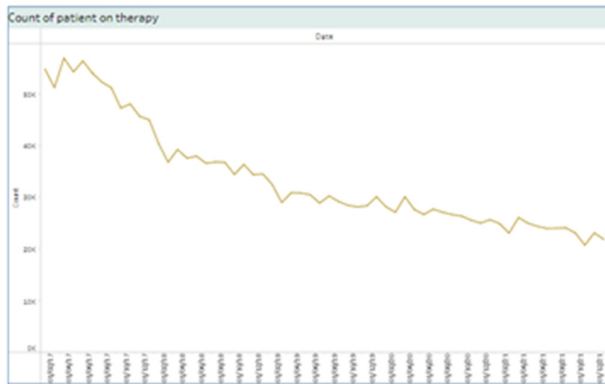
Source: Credit Suisse Healthcare Database

**Figure 78: Count of time on therapy for Invokana patients**
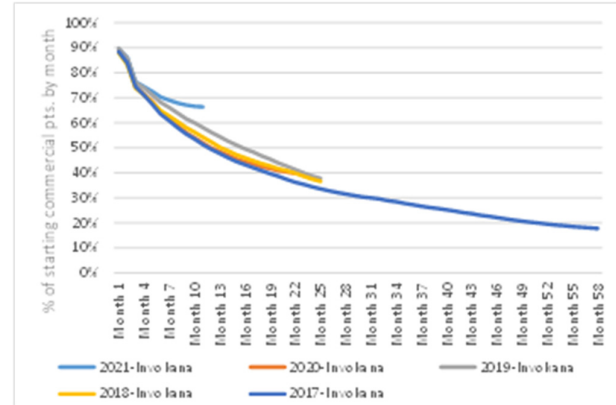
Source: Credit Suisse Healthcare Database

Figure 79: Invokana median co-pay by channel, 2015-2021
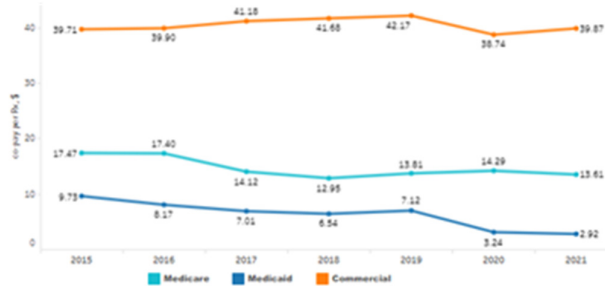
Source: Credit Suisse Healthcare Database

**Figure 80: Funding by age and overall funding, 2021 for Invokana**
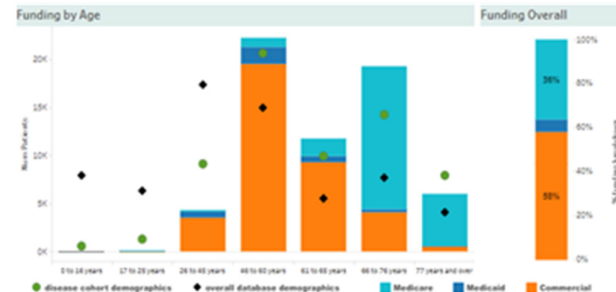
Source: Credit Suisse Healthcare Database

Patient flow

On patient flow into Invokana in 2021, there is a wide range of prior therapies. In this data set, of the patients who either switched to or added Jardiance in 2021, c.7% started without prior therapy (within this data set) and 19% added Jardiance to an existing regimen. For straight switches, the data shows c.4% moved from metformin, c.2% from Jardiance and c.2% from Januvia.

When we look at patient flows away from Invokana in 2021, we see c.54% of patients that completed six months of treatment remaining on therapy for a full 12 months. The rest of the patients changed therapy: c.4% moved to GLP-1 therapies, c.9% moved to other SGLT-2 therapies, c.5% moved to metformin and c.22% discontinued this treatment.

Figure 81: 2021 patient flows to Invokana

Figure 82: 2021 patient flows from Invokana
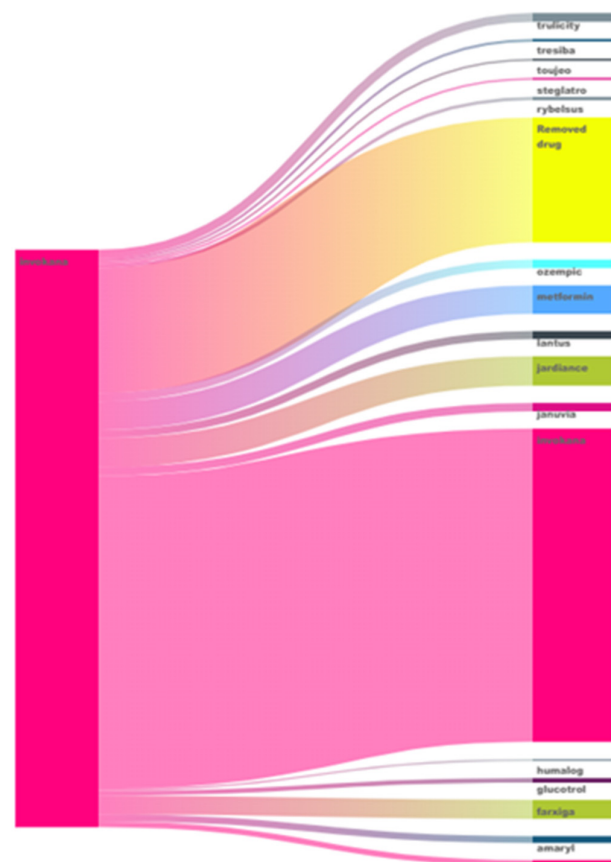
Appendix

Appendix 1: Introduction to diabetes

Diabetes is a chronic disease that causes the inability to manage blood sugar levels appropriately. Type 2 diabetes (non-insulin-dependent diabetes) makes up the majority of the disease. According to the WHO, more than 400m adults worldwide have diabetes today, and this is expected to increase to 700m by 2024 (+51%).

Although several effective therapies are available today, many patients' management of the disease wanes over time, and they need to add more therapies or switch to new therapies to control glycaemia appropriately. With time, we have seen new classes of drugs come to the market, which offer both better blood-glucose control and better management of weight and other co-morbidities of the disease (Figure 83).

Today, the typical treatment algorithm for Type 2 diabetes patients is:

After a failure of diet and exercise, patients are first prescribed metformin.

Patients then move to alternative and oral antidiabetic medicines (various drug classes, SU (sulfonyl ureas), DPP-4 (Dipeptidyl-peptidase 4 inhibitors), SGTL2 (Sodium-glucose cotransporter 2), and most recently the first oral GLP-1 (Glucagon-like peptide-1). These newer drugs may be given alone or more commonly in combination with metformin.

Diabetes is controlled but not cured by this medication and as it progresses and patients fail to control their blood sugar levels, they typically move to more intensive therapy including the option of an injectable GLP-1 therapy.

When all the above treatments have failed, patients are given insulin as the last-line option. Insulin is unfavourable for patients as the therapy causes weight gain.

We illustrate the ability of various classes of diabetes medicine to lower blood sugar in Figure 86 (horizontal scale and the impact on patent weight in the vertical scale). Insulin is seen as the ultimate treatment for Type 2 diabetics when blood sugar levels are not controlled by other treatments, but this figure also highlights that insulin typically leads to weight gain when all the advice a patient gets is to lower weight.

In contrast, the GLP-1 class lowers weight with increasingly potent treatments available that lower both blood sugar significantly and weight. GLP-1s also benefit from lower side effects – specifically, these do not cause hypoglycemia, which is a potentially serious side effect of insulin treatments.

In Figure 84, we illustrate the importance of the diabetes category to various companies in terms of their percentage of group NPV (vertical scale) and to the overall market (horizontal scale). Novo Nordisk has the highest exposure to this category of diabetes and contributes the most to the overall category. This may change with the full approval of tirzepatide (Lilly).

The diabetes market is characterised by very high levels of competition, which can be seen in the growing difference between gross and net sales for key drugs, as illustrated in Figure 85.

Figure 83: Diabetes is a chronic disease requiring intensifying treatment over time
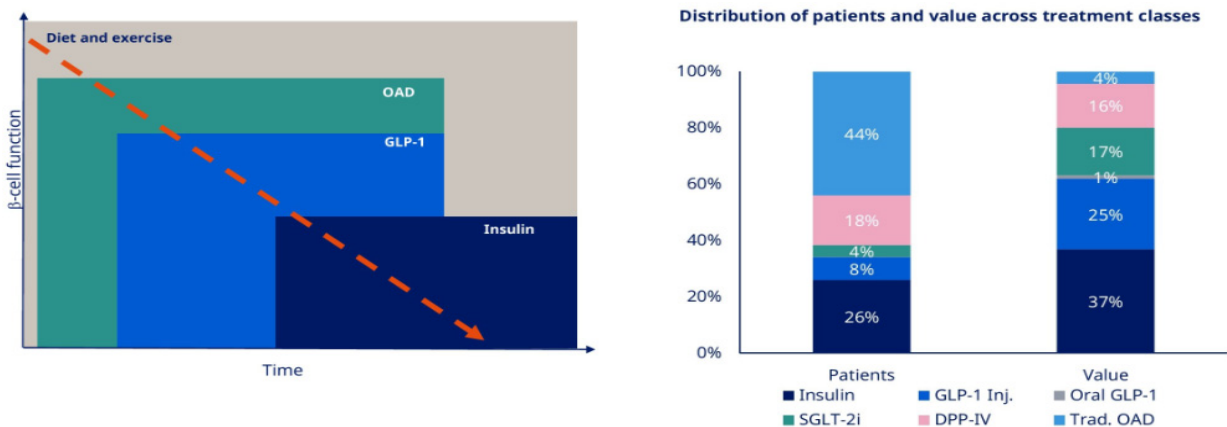
Note: Patient distribution across treatment classes is indicative and based on data for the USA, Germany, France. Other OADs cover: metformin, sulfonylurea, thiazolidinediones.
Source: IQVIA PharMetrix claims data, IQVIA disease analyser, IQVIA MIDAS; value figures based on IQVIA MAT, Nov 2021
OAD: Oral anti-diabetic

Source: Novo Nordisk FY2021 investor presentation

Figure 84: Credit Suisse PharmaValues analysis of the diabetes market highlights the contribution of diabetes to major quoted companies, and the importance of each company in the market
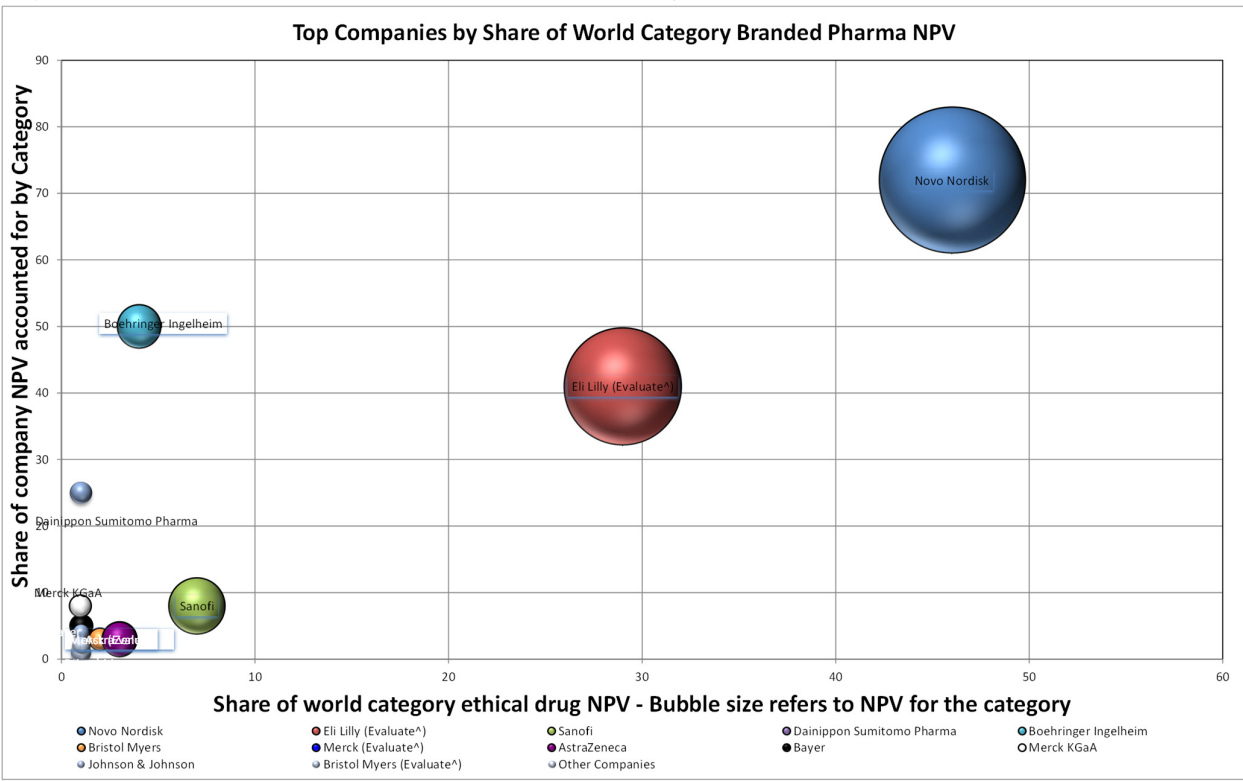
Note that for some US majors where we have no current analyst coverage, drug forecasts are taken from Evaluate Pharma; Source: Credit Suisse PharmaValues analysis

Figure 85: US gross and net price per day for leading companies in each of the key classes of diabetes drugs
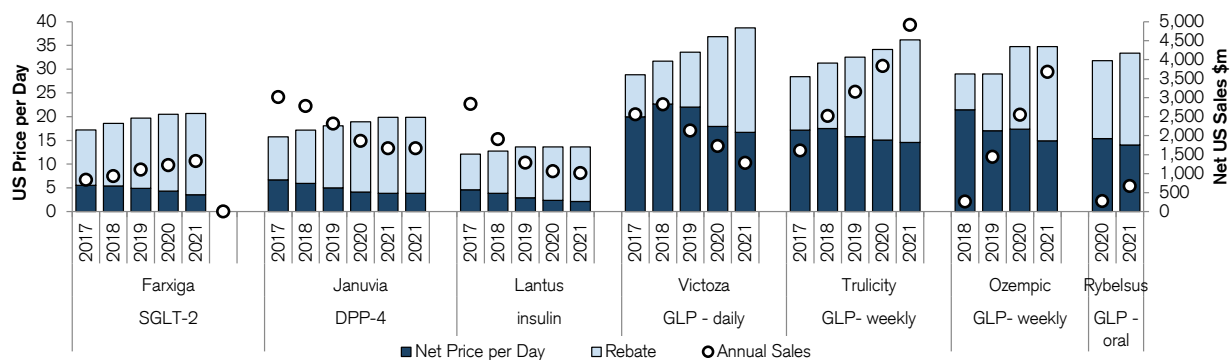
Source: Company data; Gross to net estimated by Credit Suisse using IQVIA gross net sales data.

Figure 86: Impact of various diabetes drugs on weight and blood sugar based on reported clinical data over the years
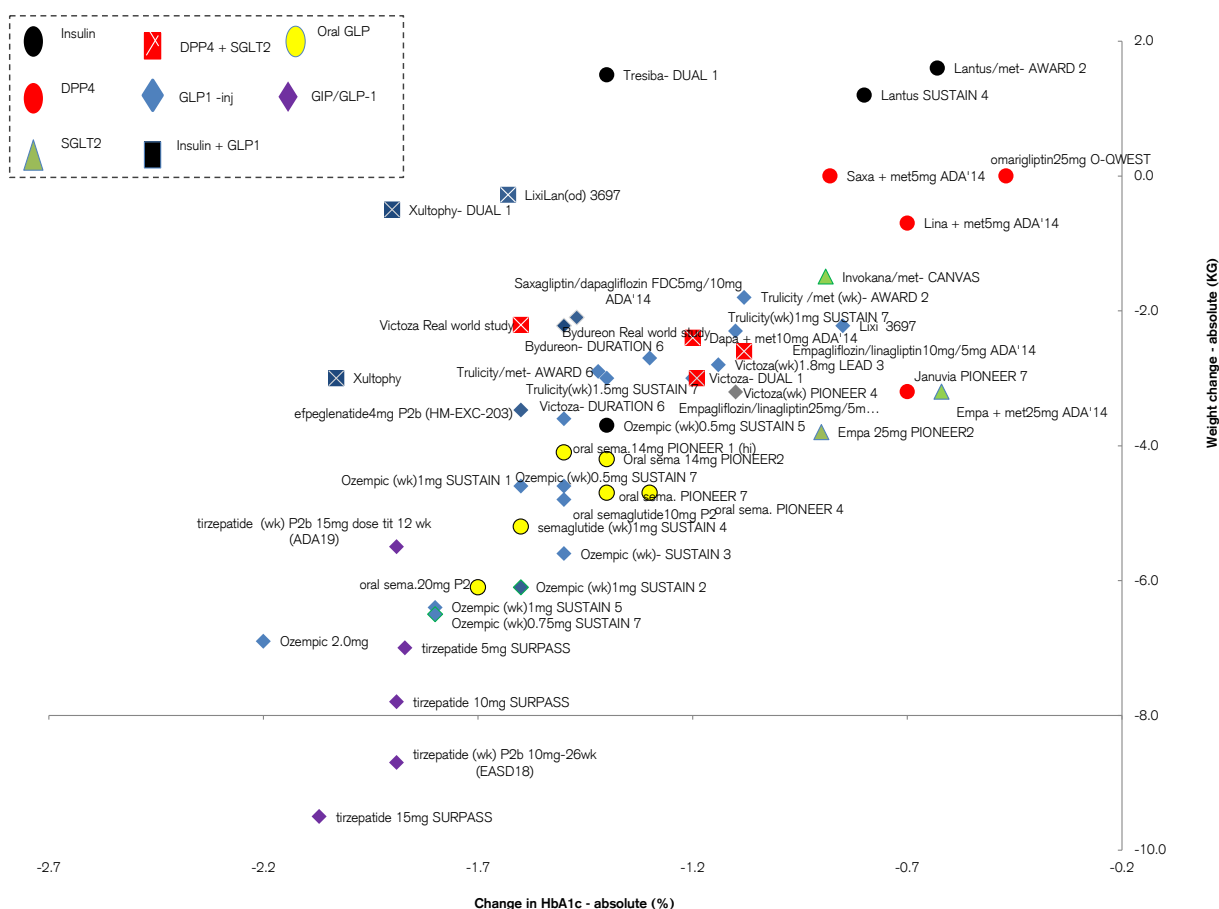
Source: Company data, Credit Suisse

Key drugs in diabetes

In this section, we introduce the key classes of drugs used in diabetes treatment today: metformin, DDP-4s, SGLT-2s, GLP-1s and insulins.

Below we present the US and Worldwide (WW) branded diabetes market size using our PharmaValues database. We estimate that the total WW diabetes market is worth c$53bn today, of which the US makes up $24bn. We expect a US market CAGR of 5% and a WW market CAGR of 3% over 2021-26 on a probability-adjusted basis. By 2027 on a probability-adjusted basis, we estimate the WW diabetes market will be worth c$62bn.

We expect the GLP-1 class to see the highest growth, at an 11% CAGR in the US and at 14% WW over 2021-26.

Metformin

Metformin is the first treatment given to patients diagnosed with Type 2 diabetes. The drug is a small-molecule oral pill that was developed by Merck KGaA in the late-1950s but

was launched in the US under licence by Bristol Myers only in the 1980s. It is now available as a generic drug globally. Various brand names include Glucophage, Fortamet, and Riomet. The drug is used very frequently in single tablet combinations with other drugs.

DPP-4s

DPP-4 inhibitors are a class of daily oral anti-diabetics that work by preventing the degradation of incretin hormones (in particular GLP-1) in the circulation. Incretins help regulate insulin and glucagon secretion in response to food (glucose) consumption. Januvia (Merck) was the first DPP-4 inhibitor approved in 2006 and remains the main DPP-4 today; however, loss of exclusivity occurs in July 2022. DPP-4 inhibitors have a broadly neutral impact on patient weight, unlike insulins that cause weight gain, or GLP-1s and SGLT-2s that result in more marked weight loss. DPP-4s are cheap and effective but do come with a level of safety concern (some associated risk of pancreatitis, gastrointestinal problems, joint pain, cardiovascular issues etc.).

Figure 87: US Branded diabetes market, probability-adjusted sales
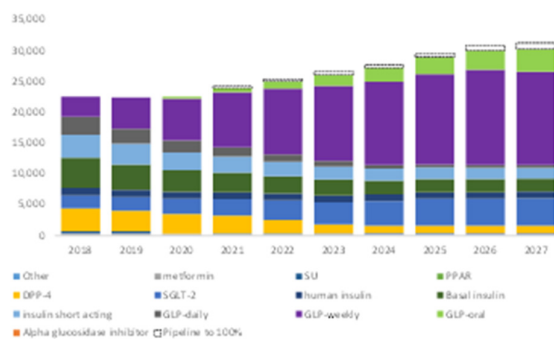
Source: Company data, Credit Suisse PharmaValues, US Major Pharma drug estimates from Evaluate consensus

Figure 88: WW Branded diabetes market, probability-adjusted sales
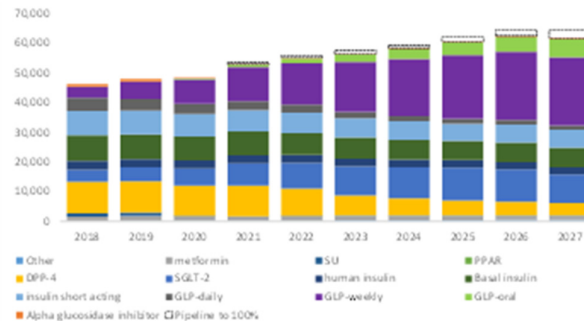
Source: Company data, Credit Suisse PharmaValues, US Major Pharma drug estimates from Evaluate consensus

Figure 89: Credit Suisse Healthcare Database transitions from metformin
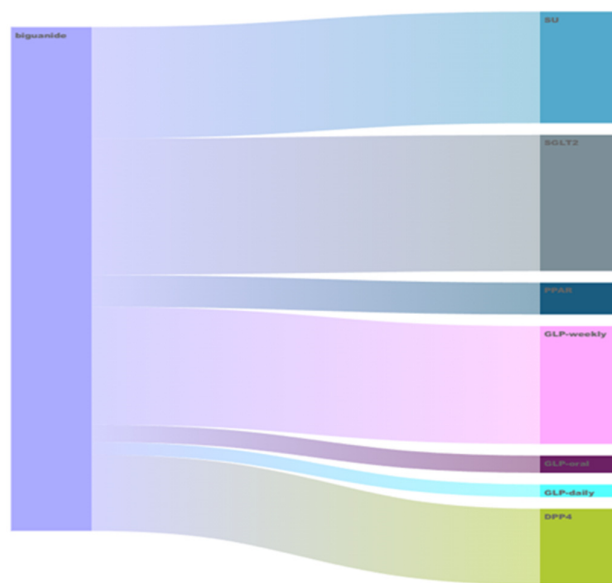
Source: Credit Suisse Healthcare database (excluding <1,000 transitions)

SGLT-2s

This class of drugs inhibits SGLT-2 proteins in the kidneys. SGLT-2 is responsible for reabsorbing glucose into the blood. This results in more glucose excretion, resulting in lower HbA1c levels (a measure of blood sugar). Along with DPP-4 inhibitors (and increasingly GLP-1s), these represent one of the main oral options for diabetes treatment after metformin and SUs. SGLT-2 inhibitors have been around for many years in diabetes but are increasingly being applied more broadly beyond diabetes with recent approvals in heart failure and chronic kidney disease. Jardiance (BMY/Boehringer Ingelheim) recently showed positive data in a Phase 3 trial in Heart Failure with preserved ejection fraction (HFpEF) and has since been approved (February 2022). AZN/BMY expect pivotal data from Farxiga DELIVER P3 trial in this setting in 1H22. The Farxiga HFpEF data showed benefit in the composite primary endpoint of cardiovascular (CV) death and hospitalisation but was driven by the hospitalisation component (not significant on survival) – this presents an opportunity for Farxiga to be the SGLT-2 of choice if it can show a significant improvement in patients' survival rates. Pricing in the SGLT-2 class is low at a net price of c$4/day for 2021 (similar to DPP-4s) vs the GLP-1s at ~$15/day. We note that the SGLT-2 class will come off patent in the latter half of the decade, with Farxiga the first to lose exclusivity, with a patent expiry in April 2026. The Jardiance patent is set to expire in August 2028 and Invokana in February 2029.

GLP-1s

A newer class of drugs called the GLP-1s has shown very good efficacy, beyond just glycaemic control (HbA1c change), with benefits of weight loss, no hypoglycaemia (seen with insulins) and some therapies also showing CV risk reduction. The first GLP-1s to the market were daily injectable therapies (e.g. Victoza) but these have been replaced more recently by weekly (Ozempic, Trulicity) and even oral formulations (Rybelsus). Over 2018-21, CS estimates suggest that the GLP-1 segment grew from $8bn to $15bn WW, while the branded insulin market fell from c$20bn to c$18bn.

A long-standing debate in the diabetes market is how long patients actually remain on these GLP-1 therapies. With currently available data sets, we have no way to see for how long patients take GLP-1s, or what therapies they take before/after taking a GLP-1 (or indeed in combination with).

A key strategy for leading GLP-1 manufacturers is to shift the use of GLP-1 earlier in the treatment paradigm given the stronger efficacy. This should in turn lead to patients taking the therapy for longer, given the chronic nature of the disease. According to data at Novo's recent CMD, 25% of patients now receive a GLP-1 immediately after metformin (up from c17% before the Ozempic launch in 2017). The Credit Suisse Healthcare Database supports this conclusion. Looking only at patients who added new treatments to metformin in 2021, we see that 23% added a weekly GLP, and 3% added an oral GLP. The most common addition was an SGLT-2 at 27% (Figure 89).

Insulins

Type 2 disease is typified by a patient producing insulin in response to the presence of blood sugar but the body becoming resistant to the insulin produced. Initial treatments increase the amount of effective circulating insulin to overcome resistance but as time goes by response often wanes and eventually patients may need to take supplemental insulin treatment. Albeit effective, it is both inconvenient as it needs to be taken via injection, and has side effects of both increased weight and potential episodes of hypoglycaemia. While Type 1 diabetics typically need insulin at meal times and may inject several times a day, Type 2 diabetics can normally manage with a single daily injection increasing the levels of circulating insulin. The main Western branded insulin manufacturers are Eli Lilly, Sanofi and Novo Nordisk. Lantus was the first long-acting basal insulin analogue to provide 24 hours of coverage (with a half-life of 12 hours), launched in 2000, followed by Novo Nordisk's Levemir in 2005. Competition has revolved around delivery devices such as room-temperature stable insulin pens, and longer-acting versions Toujeo from Sanofi (2015) and Tresiba from Novo (2016). Sanofi has more recently exited new drug development in diabetes but Novo continues to innovate both in GLP-1s and in insulin with the possibility of a once-weekly insulin from Novo Icodec. We expect to see the first data from the P3 insulin Icodec programme this year.

Appendix 2: The Credit Suisse Healthcare Database

The Credit Suisse Healthcare Database contains more than seven years of prescription (Rx) and medical (Mx) claims data from well over 100m anonymised US patient records over this time frame. Using this extensive database, we have been able to develop a unique insight into typical therapeutic journeys through various diseases. Where other Rx audit services can provide no continuity of patient coverage, this database allows us to look at transitions from one treatment to another and detail typical drug cocktails in any year, all of which may give us a better idea of the treatment burden for a disease and likely patient costs.

We can also look at treatment persistence (length of time on a treatment) and compliance (number of claims made in chronic diseases versus expected claims for 100% compliance). These together may give us an idea of patient satisfaction with a treatment and help define market penetration, both important for modelling sales.

The overall enrolment data in the Credit Suisse Healthcare Database covers over 122m unique member IDs active in 2021. There were just over 113m active subscribers on average in each quarter of 2021. We have claim and funding status data on 61.9m enrollees who made claims in 2021. A total of 63.8m unique claimants are identified, suggesting that we are missing contextual data on only 3% of claimants.

We have seen a rise in claimants for Rx services in line with enrollee numbers, with a much more stable medical claims base. We note the lack of increase in active subscribers claiming for diabetes prescriptions or medical claims, but still see broad correlation with other audit services for key drugs. We note the higher lag time for medical claims being available to us and believe this may partly explain the reduction in medical claims in 2021.

Strong correlation of Rx trends with other audit services

Trends we see in patient counts in this database for the chronic outpatient prescription treatments seem to accord reasonably well with broadly equivalent Total Prescription Data (TRx) data reported by other prescription services such as IQVIA over the period 2017 to 2021.

The Credit Suisse Healthcare Database data set is based on claims rather than being sampled at the point of being dispensed, and therefore does not match IQVIA for speed of reporting. However, we can see some Rx data for rarer diseases and hospital-delivered drugs within the Credit Suisse Healthcare Database where specialty pharmacy services may not be as accessible for other audit services.

In Figure 93 to Figure 96, we show the Credit Suisse Healthcare Database data scaled to the full US population and compare it to IQVIA TRx data across the key drug classes. This shows a strong correlation with IQVIA for GLPs, SGLT-2s and DPP-4s, albeit less so for insulins.

We also illustrate this correlation in Figure 2 to Figure 9 where we compare monthly patient data from the CS Healthcare Database and weekly Total Script data (TRx) and New to Brand data (NBRx).

Figure 90 Credit Suisse Healthcare Database: Insights from healthcare claims of c122m US citizens

Year	Overall Subscribers	Subscribers	Subscribers with claims	Overall Claimants			Diabetes Claimants		
				Rx	Mx	of which Rx & Mx	Rx	Mx	of which Rx & Mx
2017	114.5	105.8	50.7	31.6	20.7	15.3	3.04	1.83	1.22
2018	112.3	104.1	53.0	32.3	20.3	15.0	2.40	1.72	1.18
2019	118.1	103.9	57.9	33.4	21.6	15.3	3.06	1.80	1.20
2020	111.2	103.0	61.2	36.0	20.4	15.0	3.20	1.71	1.21
2021	121.9	113.1	61.9	43.6	20.3	15.6	2.88	1.33	0.96

Source: Credit Suisse Healthcare Database (Rx claims = prescription claims, Mx claims = medical claims)

Figure 91: Credit Suisse Healthcare Database patient Rx claims by key class in diabetes
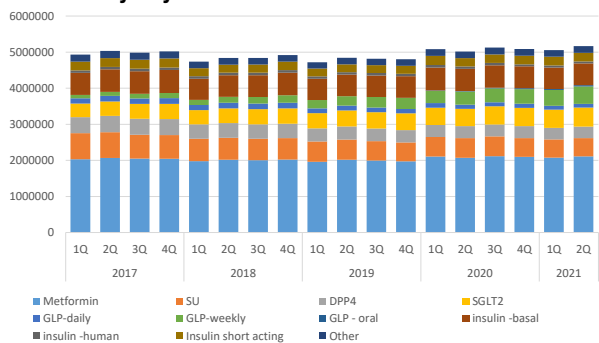
Source: Credit Suisse Healthcare Database

Figure 92: IQVIA TRx by key drug class in diabetes
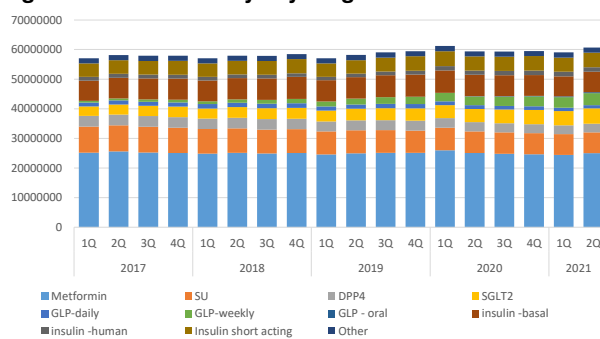
Source: IQVIA data

Figure 93: GLP-1 CS database vs IQVIA TRx
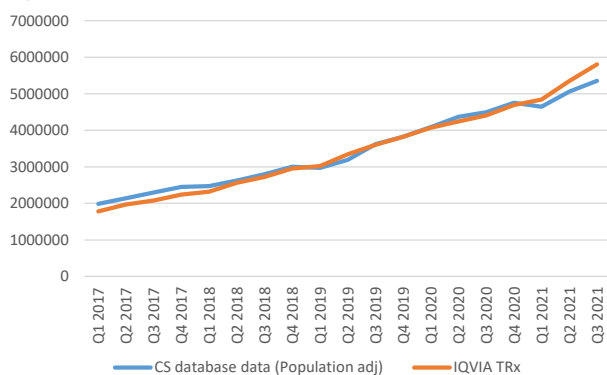
Source: Credit Suisse Healthcare Database, IQVIA audit data, Company data

Figure 94: SGLT-2 CS database vs IQVIA TRx
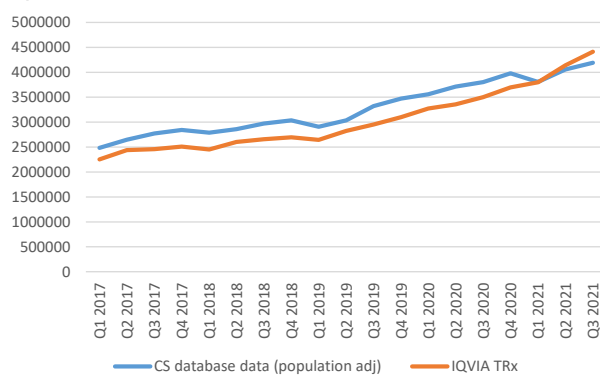
Source: Credit Suisse Healthcare Database, IQVIA audit data

Figure 95: DPP-4 CS database vs IQVIA TRx
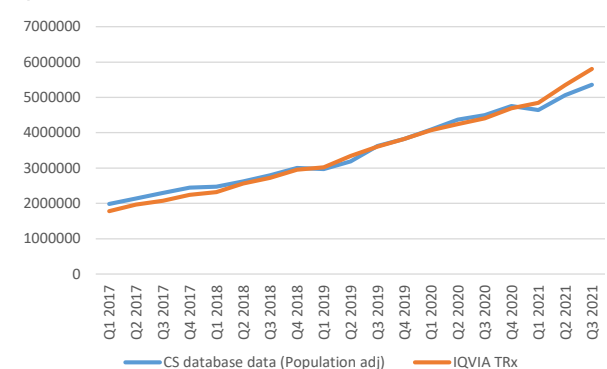
Source: Credit Suisse Healthcare Database, IQVIA audit data

Figure 96: Insulins CS database vs IQVIA TRx
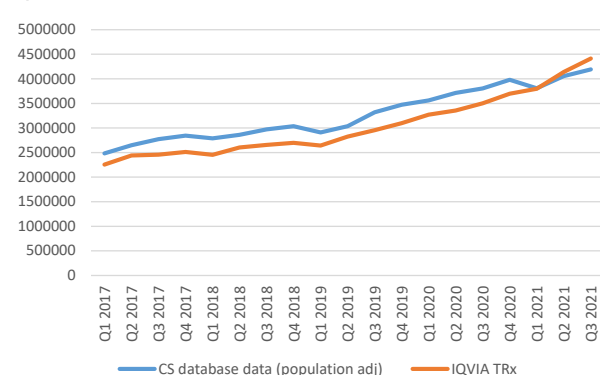
Source: Credit Suisse Healthcare Database, IQVIA audit data

Medical claims lag may limit assessment of procedure versus drug share

We have received four downloads of the claims data that underpins the Credit Suisse Healthcare Database data. There has been very strong consistency in the Rx data feed at each download, although we note a material lag in reporting the medical claims data. This suggests that the downward trend in medical claims evident in the database towards the end of 2021 is not 'real' and would be adjusted upwards with subsequent data feeds.

We note this as a limitation in comparing market shares for treatments delivered under medical as opposed to pharmacy benefits in our analysis when looking particularly at 2H21 data. This is not an issue with our diabetes analysis but could be a confounding factor looking at some other disease categories.

Figure 97: Number of medical claims over time. Note the restatement upwards for the last few months with each download

Source: Credit Suisse Healthcare Database
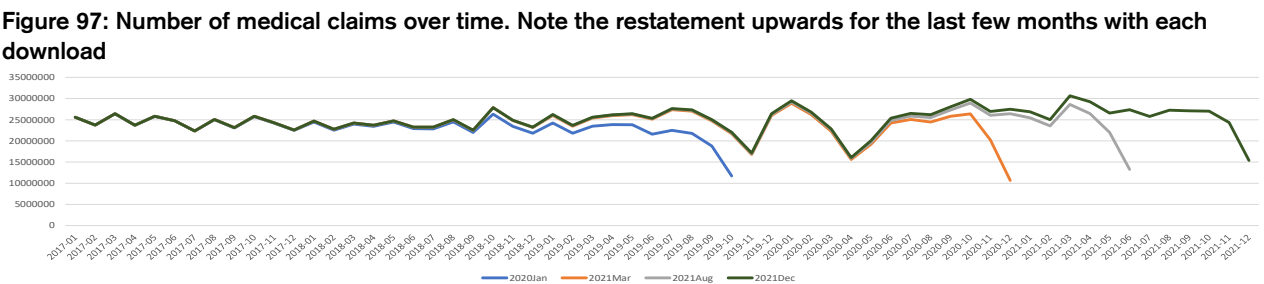
Appendix 3: Methodology of Credit Suisse analysis

Diabetes first disease analysis

We have chosen to look at diabetes as a first disease class to showcase the Credit Suisse Healthcare Database. We have made each analysis based on detailed longitudinal claims data for a cohort of patients who we group into a disease panel. For each treatment, we analyse the utilisation against both the overall panel of diabetes claimants and the overall database of subscribers. We do this analysis by age cohort, specifically highlighting patients aged 61 to 65 who currently are too young to be eligible for Medicare. We highlight this cohort so we can better understand the impact of any policy changes ahead that could extend enrolment of this age group into Medicare. We believe the database to be representative of the US population in age and healthcare funding status.

The overall database includes c122m patients as of 2021, up from 114.5m in 2017.

We have detailed data on claims from 50m people in 2017 rising to 61.9m in 2021. These subscribers have made either prescription (Rx) or medical (Mx) claims, or both.

In this analysis, we have looked solely at Rx claims for diabetes and so our diabetes panel contains 2.88m patients in 2021. This is surprisingly lower than the 3.04m diabetes claimants seen in 2017. We see this as noise rather than as a real trend. We do see growth in claimants for key drugs over time.

Underlying claims data that we can see

Each prescription is coded for the number of days of treatment covered. For chronic medication, unsurprisingly, the main Rx claims are for 30-day and 90-day prescriptions. We have been surprised at the apparently high proportion of 90-day scripts given to patients who had made no prior relevant claims and appeared to move straight to three-monthly treatment (see section on time on treatment). We assume this may reflect some initial use with free samples provided by the manufacturers to doctors as these would not be subject to claims.

We have access to co-pay data for prescriptions split by funding status (Commercial / Medicare /Medicaid) but only limited contextual data for medical claims beyond the timing of service delivery for claims, which we have tracked using J codes. We do not know to what extent the reported patient co-pay data can be offset by manufacturer co-pay assistance programmes, available only to commercially funded patients.

The vast majority of the medical claims cover physician consultation and broader service-based medical procedures (e.g., childbirth) and we have not focused on them. We have restricted our current analysis to disease-specific treatments identified under J codes (for infusions) or ICD 10 codes (for diseases) or HCPCS codes (for specific services) where we are looking at high-value drug treatments. We can only capture drugs or procedures covered by a specific J code, and analysis is limited where the diagnosis code in the claim is not specific as to the precise reason for use.

Disease panels

For each disease area we are studying, we have started by identifying all of the unique patients within the Credit Suisse Healthcare Database who have carried a relevant diagnosis at any point since 2017. A patient is counted if they have submitted a claim for one of the reference drugs or procedures we have set as defining the parameters of research in each disease. Where relevant, we have grouped drugs into sub-categories to analyse overall patient flow, and so we can look at the data at either a high level or on a more granular basis comparing competing drugs in any class. We have then created a number of views centred on patient flows.

We have allowed for short breaks in claims of three to six months depending on both the disease area and the typical length of treatments. Credit Suisse Healthcare Database Rx claims include data on the number of days the treatment should cover and we allow greater breaks between 90-day scripts than between 30-day scripts before determining a permanent change in treatment.

For each disease panel, we have also looked at the top 10 co-morbidities. This provides some context on other claims being made and may help provide an insight into overall treatment/healthcare funding burdens for patients. So far, we have seen little variation by disease.

In our analysis, we have chosen to specifically highlight the cohort of patients aged 61-65 as there have been periodic proposals to expand the eligibility of Medicare (largely used by seniors) to younger populations. Commercial plans often adopt newer treatments faster than Medicare plans and we have seen in our diabetes analysis a greater use of generic drugs in older patients.

With knowledge of the current relative utilisation by age and funding status, we can better understand the likely negative impact on branded drug sales of a move to expand Medicare eligibility to a younger population. Conversely, by looking at the current use in commercial plans, we can estimate the potential uplift in sales assuming that over time Medicare plans allow greater branded drug use at similar co-pays.

When we look at drugs for this analysis, we have aggregated brand and generic name scripts under the predominant brand name, as we want to look at transitions between molecules. We continue to use the brand name post patent expiry to avoid showing transitions in treatment that are not changes in underlying active ingredients.

We illustrate a disease panel looking at the data for Type 2 diabetes using 2021 data.

Figure 98: Funding status by age in 2021
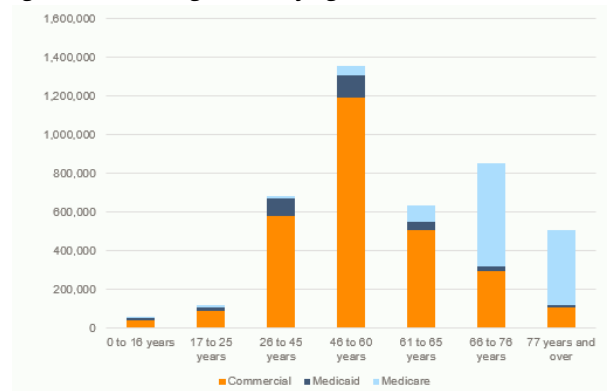
Source: Credit Suisse Healthcare Database

Figure 99: 2021 funding by age band
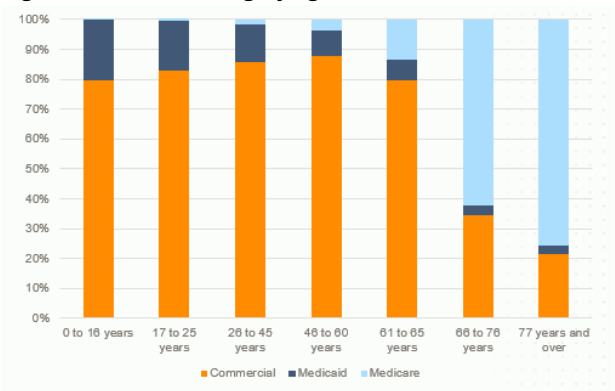
Source: Credit Suisse Healthcare Database

Figure 100: Breakdown of diabetes panel by year of joining (data to June 21 hence the apparent decline in the 21 cohort)
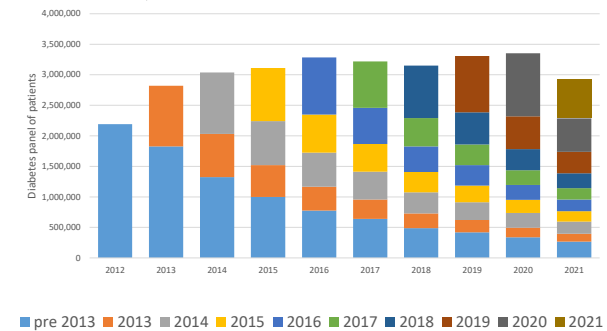
Source: Credit Suisse Healthcare Database

Figure 101: Funding status over time (to 3Q2021)
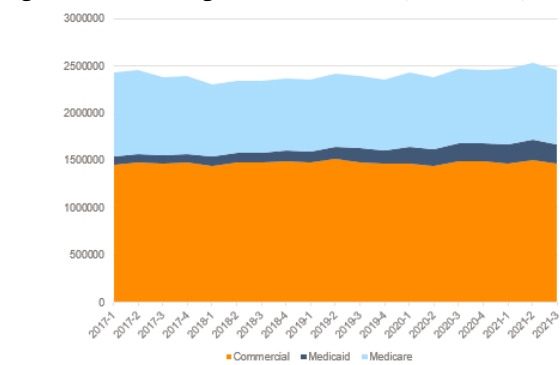
Source: Credit Suisse Healthcare Database

Counts of patients on therapy

These charts show the number of patients in the Credit Suisse Healthcare Database taking any specific drug in any month from January 2017 to end-2021. It is important to note that this reflects any person receiving that therapy at that point of time. Over the period of any year, there will be many more patients who have taken the drug for some time than will be seen at either the start or end of any year. We note that many patients claim for only one or two prescriptions (see time on treatment data); these will be counted only in the month when they received the Rx. The trends in count of patient data for diabetic drugs accord reasonably well with the trends in Rx data seen in other Rx audit data (Figure 91 and Figure 92). Overall, we believe this database captures around one-third of the US population and patient numbers need to be scaled up accordingly.

Time on treatment

In this analysis, we look at the persistence on treatment of patients who started treatment on GLPs (injectable and oral) and for comparison Farxiga as an oral SGLT-2. We show the data both in terms of numbers of patients who stopped in each month (Figure 103 and Figure 104) and in terms of the percentage of persistence of treatment. We also look at the other side of this, looking at the percentage of patients who started treatment in a specific year who are still on treatment at various time points post initiation. In this analysis, we allow for a break of four months at any point

without resetting the patient to a new treatment cycle. This allows some leeway in patients, taking into account when they may claim for a three-month script.

We analyse the typical length of treatment counting both from the start of treatment and from Month 3, therefore excluding the high rate of initial abandonment. We note that on either metric we do not see real-world persistence at the same level as disclosed by Novo or Lilly.

In Figure 103 and Figure 104, we compare the persistence of Trulicity stating in 2017 with that for Ozempic starting in 2019 (first launched February 2018). In each case, the blue bars represent patients who have genuinely stopped treatment and the orange bars those patients who are still taking the drug but who have reached the end of the database, in this case December 2021. For a patient starting Trulicity in January 2017 who takes three months' scripts, this could be up to 63 months (5 x 12 + 3) allowing for a three-month script.

In this analysis, we include only those patients who started treatment in the specified year *and* who remained active subscribers in 2021. We did this to ensure that we did not count any patients who appeared to drop off treatment because they left the database rather than genuinely transitioned away from treatment; in some cases, this cuts the available sample size significantly.

Figure 102: Count of patients on treatment over time
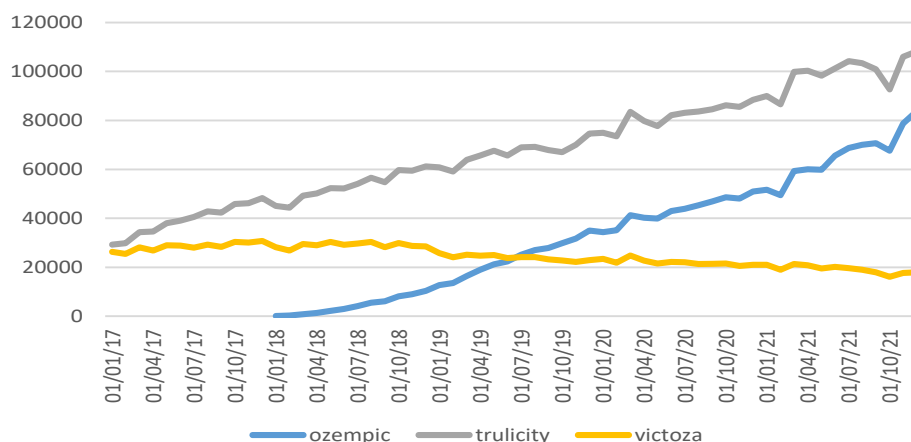
Source: Credit Suisse Healthcare Database

Figure 103: Persistence on Trulicity starting in 2017
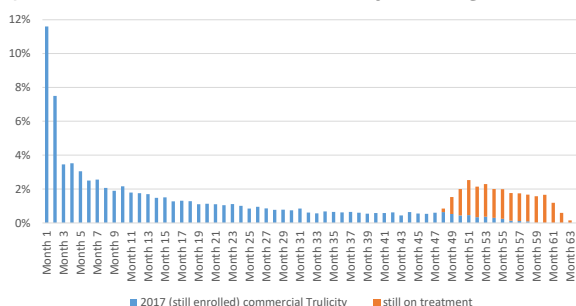
Source: Credit Suisse Healthcare Database

Figure 104: Persistence on Ozempic starting in 2019
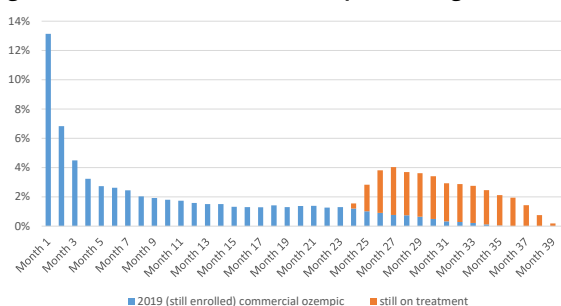
Source: Credit Suisse Healthcare Database

To measure persistence in treatment, we have looked at the drop-off for each drug (Figure 105 onwards). In each case, over 10% of patients do not make a second claim; therefore, the first datapoint at Month 1 is c.90%. We see similar persistence for Trulicity and Ozempic and Farxiga but lower persistence for Victoza and Rybelsus.

Novo quotes a stay time of c.50 months for Ozempic at 3Q21, which we assume is based on matching Trulicity stay times as Ozempic was launched only in February 2018 (only 45 months available to end-2Q21). This compares with Novo indicating a 36- to 42-month stay time on Victoza.

In Figure 109, we show the number of months it takes for 50% of patients who initially started treatment in a specific year to drop off treatment. We have looked at this both from the time of starting treatment and from Month 4, counting as starters only those patients who have completed three

months of therapy. In neither case do we get anywhere close to a persistence of treatment that matches the data quoted by Novo.

Sankey plots and how to read them

We used Sankey plots to look at treatment transitions. These tell us about both prior and subsequent treatment regimens for patients who transition from one drug (or drug cocktail) to another over any specified year. In this section, we detail how to read a Sankey plot.

We have at least two Sankey plots for each drug in our analysis, the first that looks at the transitions from other treatments to the relevant drug /procedure over any given year and a second Sankey plot that looks at the transitions away from the relevant drug /procedure.

Figure 105: Persistence on treatment for Trulicity
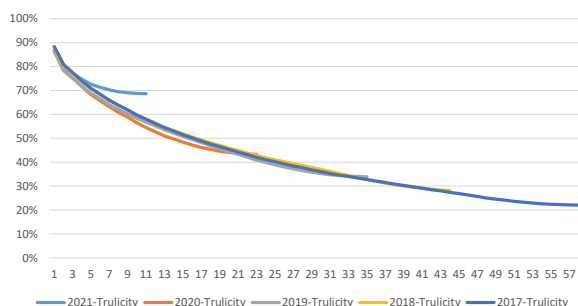
Source: Credit Suisse Healthcare Database

Figure 106: Persistence on treatment for Ozempic
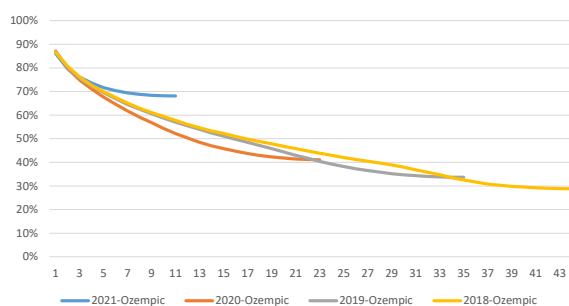
Source: Credit Suisse Healthcare Database

Figure 107: Persistence on treatment for Victoza
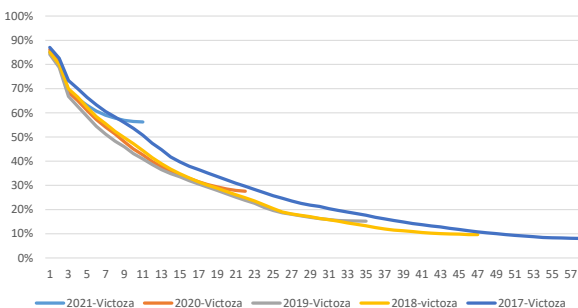
Source: Credit Suisse Healthcare Database

Figure 108: Persistence on treatment for Farxiga
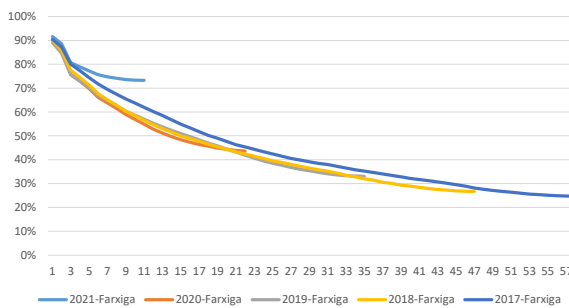
Source: Credit Suisse Healthcare Database

Figure 109: Months to a 50% drop-out of commercial patients from either start of treatment or from Month 4

From	class	2017		2019		2020	
		Start	Mth 4	Start	Mth 4	Start	Mth 4
metformin	oral biguanide	15	27	9	20	8	17
Trulicity	Weekly GLP inj.	16	27	16	27	13	58% at 23 mths
Ozempic	Weekly GLP inj.			16	27	13	55% at 23 mths
Farxiga	oral SGLT2	18	27	16	25	14	57% at 23 mths
Invokana	oral SGLT2	12	22	16	24	12	53% at 23 mths
Jardiance	oral SGLT2	23	35	18	30	15	60% at 23 mths
Victoza	Daily GLP inj.	11	15	8	15	8	15
Rybelsus	oral GLP					7	15

Source: Credit Suisse Healthcare Database

It is important to note that patients are counted in this analysis only if they take the relevant drug for at least six months. We know that many patients may take a drug for six months within a year but drop off treatment before the year-end. We therefore typically see a higher number of patients who transition onto a drug than we see as patient counts at the end of the year. The Sankey plots show patients taking a drug in both monotherapy and in combination with other drugs and there will be double-counting when a patient transitions to multiple drugs.

We illustrate these Sankey plots using Ozempic in 2021 as an example.

Patient transitions onto a drug (Figure 110). Here on the left-hand side, we have the prior therapies taken by patients who subsequently went on to take at least six months of therapy of Ozempic at some point in 2021. In addition to more obvious transitions from named drugs, we see "added drug" where Ozempic has been added to an existing unspecified cocktail and "started drug" where the patient has submitted a claim just for this drug. A patient can complete the necessary six months of treatment at any point during the year and will then count as a drug transition even if they have moved away for the drug later in the year.

Patient transitions away from a drug. When looking at transitions away from the drug, the same rules apply. In moving to a new treatment regime, a patient only counts when they have been stable on any new regime for six months and if they did not complete the six months moving to a drug of choice until beyond June, they will not have completed six months off the drug and will still be deemed to have settled on a new therapy. "Removed drug" may reflect a drug being removed from an existing cocktail and does not necessarily indicate no treatment at all.

Patient stays on a drug. Where a transition is deemed to be from the drug in focus to the same drug, this will reflect only those patients who have completed the full year on the drug (allowing for up to a four-month break in treatment). If a patient has completed the six-month qualifying period only in, say, September, they will have only a further three months of treatment before the end of the year and will not be seen as completing a full six months of therapy.

All drugs are referred to by the original US brand name even when they are now generic, although metformin is referred to only by its generic name throughout. We include fixed dose combinations with metformin under the key drug name, for example Invokana includes Invokanamet. To improve the clarity of the charts, we can set a threshold for any chart of transitions we consider "noise". In the case of Figure 110 and Figure 111, this is set at 500.

Figure 110: Transitions of drugs to Ozempic in 2021

Source: Credit Suisse Healthcare Database (excluding <500 transitions)

Figure 111: Transitions from Ozempic to other drugs in 2021

Source: Credit Suisse Healthcare Database (excluding <500 transitions)

Figure 112: Worked examples of transitions in Sankey plot analysis

Patient treatment	2019	2020	2021	How patient is treated in Sankey plot analysis

patient completed 6 months on drug A having started in 2019 — This will be counted as transition to Drug A in 2019. As the patient started takir... and continued on it ever since. Even though the completion of 6 month pe...

patient completes only 5 months on drug A in 2020 then no treatment — only 5 months of data so not a transition to drug A.

patient completes 6 months and then after a 6 month gap starts new treatment for 2 months — In this case, the patient will be counted as transition to drug A in 2019. Transit... nothing (Removed drug). Transition from nothing to Drug B (new add). Even tho... only on drug B for 2 months in the year 2020, we look for a 6 month window e... to see if the patient continued for at least 6 months, which in this case is true... consider drug B as a **new start** in 2020 (time period when the patient sta...

patient completes 6 months (allowing for drug holiday) and then after a 6 month gap starts new treatment for — Counted as transition to Drug A in 2019. Normalization will be used to account...

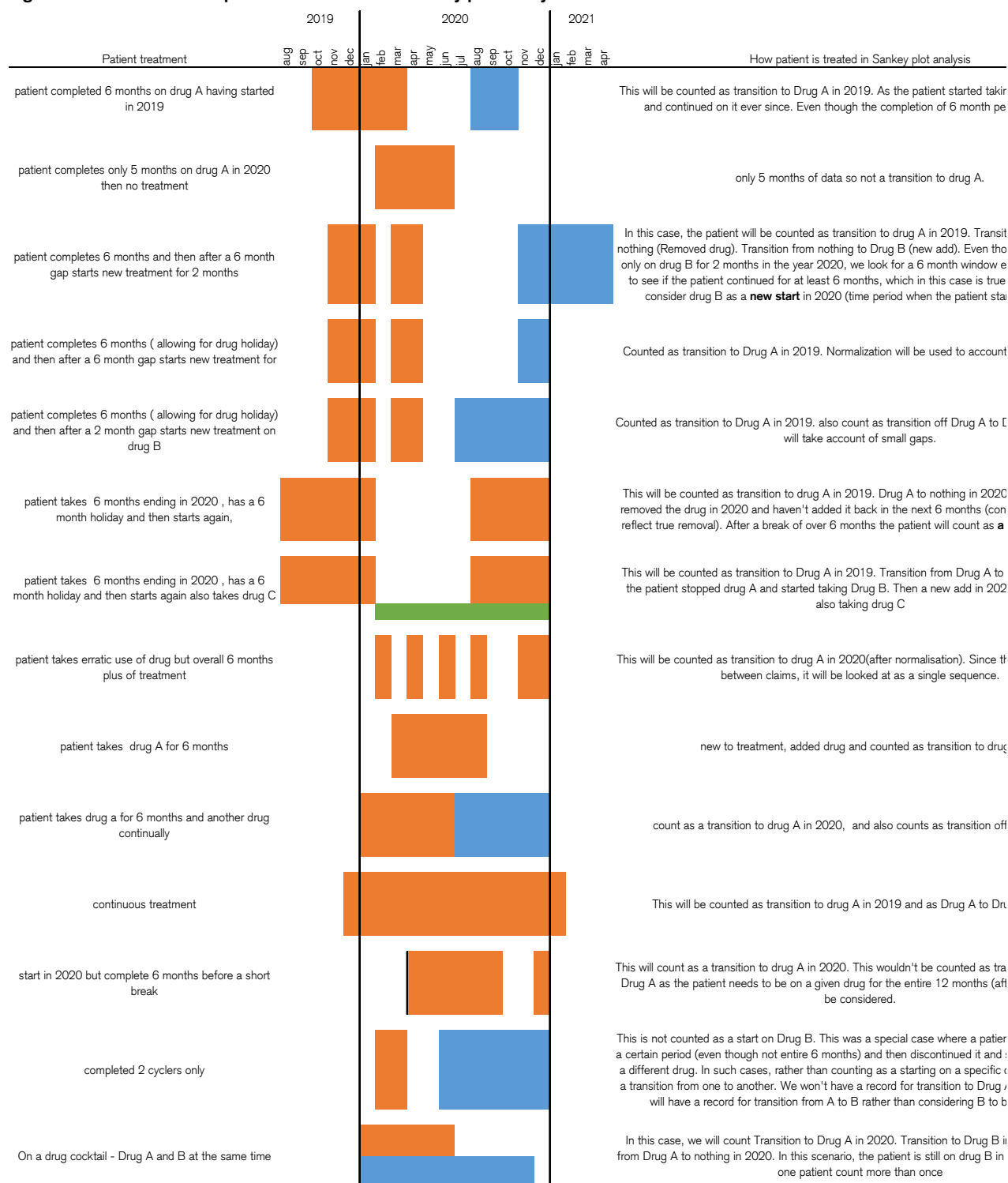patient completes 6 months (allowing for drug holiday) and then after a 2 month gap starts new treatment on drug B — Counted as transition to Drug A in 2019. also count as transition off Drug A to D... will take account of small gaps.

patient takes 6 months ending in 2020 , has a 6 month holiday and then starts again, — This will be counted as transition to drug A in 2019. Drug A to nothing in 2020... removed the drug in 2020 and haven't added it back in the next 6 months (con... reflect true removal). After a break of over 6 months the patient will count as **a**...

patient takes 6 months ending in 2020 , has a 6 month holiday and then starts again also takes drug C — This will be counted as transition to Drug A in 2019. Transition from Drug A to... the patient stopped drug A and started taking Drug B. Then a new add in 202... also taking drug C

patient takes erratic use of drug but overall 6 months plus of treatment — This will be counted as transition to drug A in 2020(after normalisation). Since th... between claims, it will be looked at as a single sequence.

patient takes drug A for 6 months — new to treatment, added drug and counted as transition to drug...

patient takes drug a for 6 months and another drug continually — count as a transition to drug A in 2020, and also counts as transition off...

continuous treatment — This will be counted as transition to drug A in 2019 and as Drug A to Dru...

start in 2020 but complete 6 months before a short break — This will count as a transition to drug A in 2020. This wouldn't be counted as tra... Drug A as the patient needs to be on a given drug for the entire 12 months (aft... be considered.

completed 2 cyclers only — This is not counted as a start on Drug B. This was a special case where a patier... a certain period (even though not entire 6 months) and then discontinued it and ... a different drug. In such cases, rather than counting as a starting on a specific ... a transition from one to another. We won't have a record for transition to Drug ... will have a record for transition from A to B rather than considering B to b...

On a drug cocktail - Drug A and B at the same time — In this case, we will count Transition to Drug A in 2020. Transition to Drug B ir... from Drug A to nothing in 2020. In this scenario, the patient is still on drug B in... one patient count more than once

Source: Company data, Credit Suisse

Funding status by channel

We plot the number of patient claims for a drug over the course of a year split by the age and funding status of the claimant. Each picture is set against a background of the demographics of our Healthcare Database represented by dots. The overall Credit Suisse Healthcare Database age profile and the disease cohort profile are scaled to match the drug use.

We have specifically highlighted the use of drugs in the 61-65 age bracket. Per capita drug use is as expected higher in this age group than the 46- to 60-year-olds, but is still largely funded by commercial plans that typically are more amenable to branded drug use and where manufacturers can still use co-pay assistance programmes to promote use. This allows us to better understand the impact of any change in healthcare funding, for example, the impact of moving patients in this age range from commercial to Medicare programmes. Looking at Figure 113 and Figure 114, we can see the changing use of Trulicity over time. In 2017, 81% of sales were commercially funded, a level that fell to 72% in 2020 and 68% in 2021. This coincides with the growing use of Trulicity in older age cohorts funded by Medicare.

The green dots in Figure 113 and Figure 114 represent the demographics of the overall diabetes panel of c3m patients in 2017 and 2.88m in 2021. The black diamonds represent the demographic breakdown of the overall database of 115m subscribers in 2017 and c122m patients in 2021.

Trulicity per capita use is much higher than would be expected in the overall diabetes population aged 46-60, and to a lesser extent for those aged 61-65, as the orange and blue bar is higher than the green dots. Conversely, Trulicity use is lower per capita than would be expected against the overall diabetes cohort in the 66-74 cohort as the green dot is higher than the orange and blue bar. This reflects the change in the funding status of patients and the lower likelihood of receiving a GLP in Medicare than in a commercial setting. The change in the relative position of the green spots in Figure 114, particularly marked in the 66-75 cohort, reflects the growth in Medicare use of Trulicity.

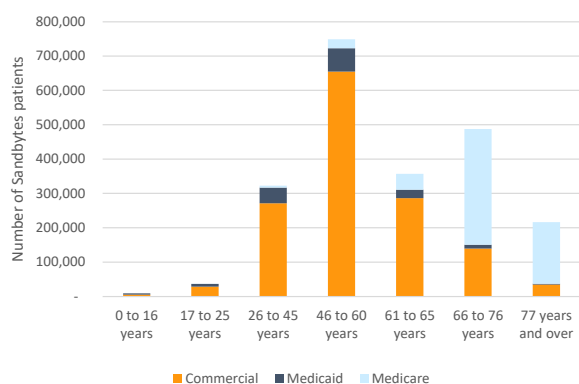**Figure 113: Trulicity funding status and per capita usage by age, 2017**
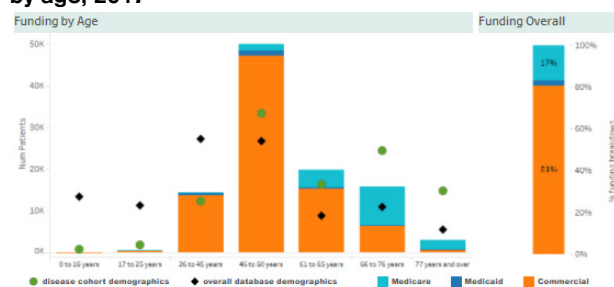
Source: Credit Suisse Healthcare Database

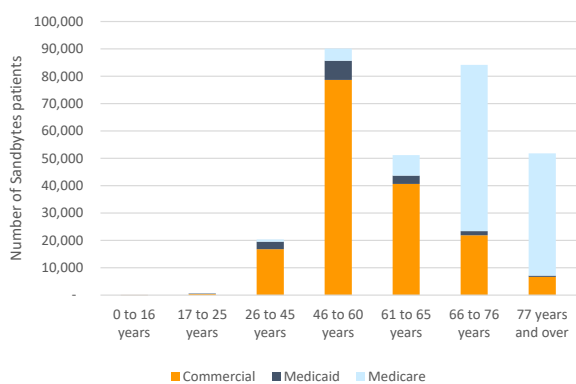**Figure 114: Trulicity funding status and per capita usage by age, 2021**
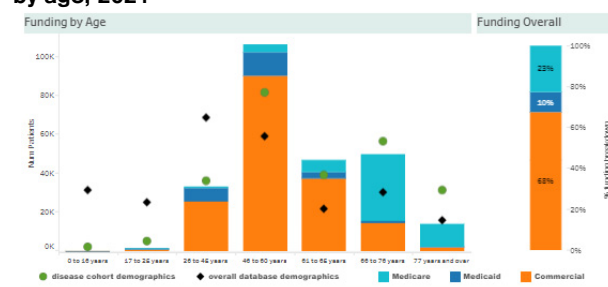
Source: Credit Suisse Healthcare Database

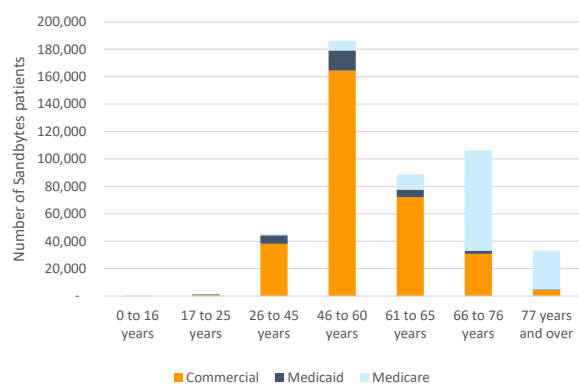**Figure 115: 2021 Metformin patients by age and payer**

Source: Credit Suisse Healthcare Database

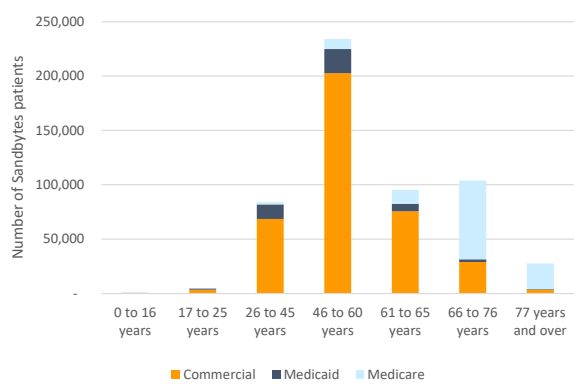**Figure 116: 2021 DPP-4 patients by age and payer**

Source: Credit Suisse Healthcare Database

Figure 117: 2021 SGLT-2 patients by age and payer
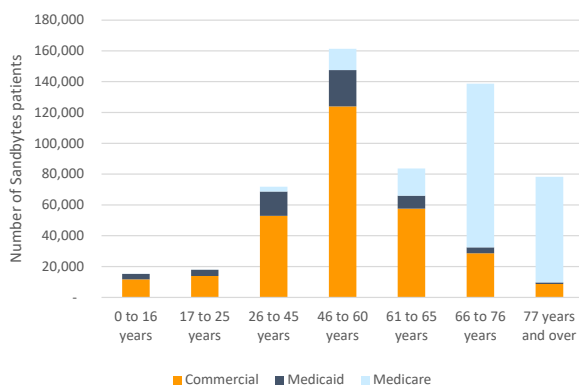

Source: Credit Suisse Healthcare Database

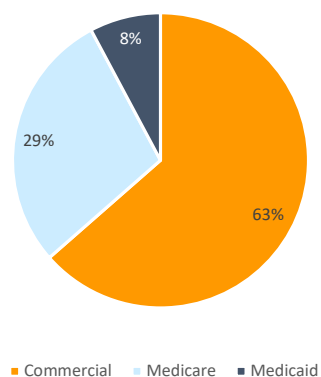**Figure 118: 2021 GLP-1 patients by age and payer**

Source: Credit Suisse Healthcare Database

Figure 119: 2021 Long-acting Insulin patients by age and payer

Source: Credit Suisse Healthcare Database

Figure 120: 2021 overall payer split in diabetes
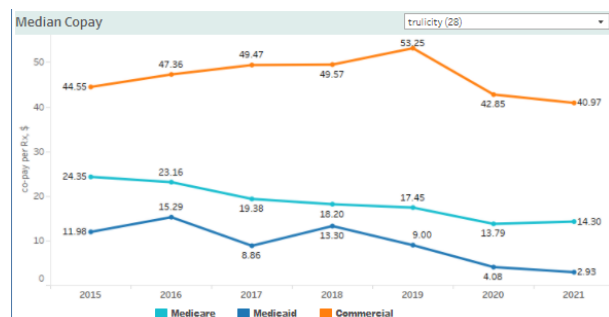

Source: Credit Suisse Healthcare Database

Median co-pay data a measure of 'financial toxicity'

We have prescription co-pay data within the Credit Suisse Healthcare Database (but no equivalent medical claims data). Commercial co-pays are universally higher than Medicare and Medicaid co-pays, but we are not sure to what degree manufacturer co-pay assistance may offset this co-pay data from a beneficiary perspective.

Manufacturers are able to provide co-pay assistance to commercially funded patients, and regularly do so with co-pay assistance cards. Manufacturers are prohibited from offering direct co-pay assistance to Medicare or Medicaid patients, but may help fund charitable foundations that support less well-off patients.
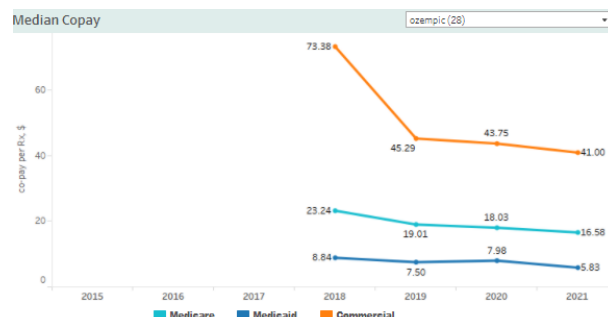
In Figure 123 we illustrate IQVIA data on prescription abandonment which clearly rises with high levels of copay.

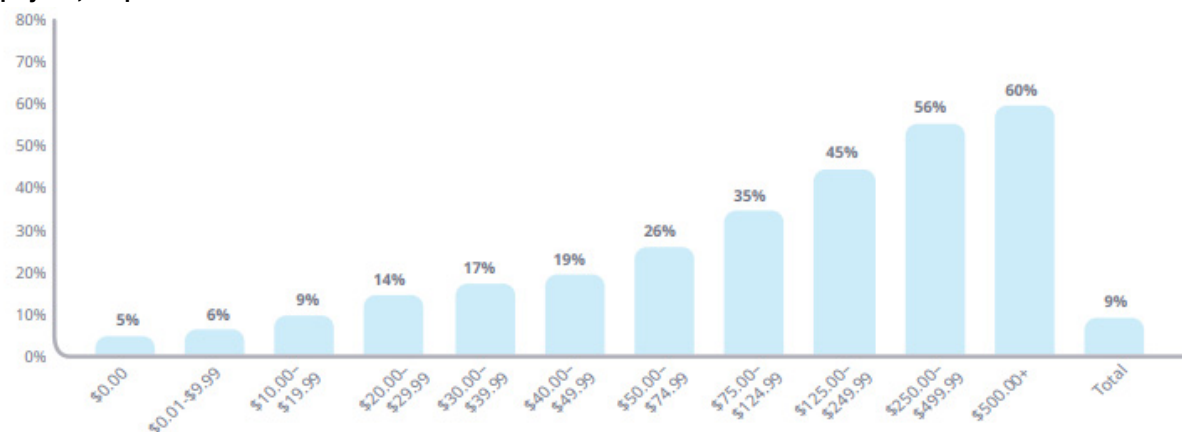**Figure 121: Median co-pay data for Trulicity**

Source: Credit Suisse Healthcare Database

Figure 122: Median co-pay data for Ozempic

Source: Credit Suisse Healthcare Database

Figure 123: 14-day abandonment share of new-to-product prescriptions by final out-of-pocket costs in 2019, all payers, all products

Source: IQVIA LAAD Sample Claims Data, December 2019. Medicine Spending and Affordability in the United States August 2020, IQVIA Institute for Human Data Science

Appendix 4: Drug reference table

Figure 124: Reference table of diabetes drugs reviewed in Credit Suisse Healthcare Database analyses, and branded drug sales

Drug class	US launch	US Patent Expiry	brand name to show	generic name to show	Main marketer	US sales	2021 U$m ex US sales	WW sales	Source
biguanide	1954	exp	metformin(Glucophage)	metformin	BMY(Merck KGaA)/generic				
meglinitide	Dec-97	Nov-13	Prandin	repaglinide	Novo/generic				
Insulin secretion enhancer	Feb-01	Sep-09	Starlix	nateglinide	Novartis/generic				
Alpha glucosidase inhibitor	Feb-15	exp	miglitol	miglitol	generic				
Alpha glucosidase inhibitor	Dec-90	exp	Glucobay	acarbose	Bayer/generic				
PPAR	Aug-99	Aug-12	Actos	pioglitazone	Lilly/generic				
PPAR	Jun-99	Mar-12	Avandia	rosiglitazone	GSK/generic				
SU	Dec-95	Oct-05	Amaryl	glimepiride	Hoeshst (Sanofi)/generic				
SU	Aug-20	Jan-04	Glucovance	glibenclamide	BMY/generic				
SU	Sep-84	Jun-94	Glucotrol	glipizide	BMY/generic				
SU	Oct-79	exp	tolbutamide	tolbutamide	generic				
DPP4	Nov-06	Jul-22	Januvia/Janumet	sitagliptin	Merck	1771	3792	5563	Evaluate
DPP4	Aug-09	Jul-23	Onglyza	saxagliptin	AZN	88	272	360	CS
DPP4	Jun-11	May-25	Tradjenta	linagliptin	Lilly/BI	1090	646	1736	Evaluate
DPP4	Sep-11	Jun-21	Oseni	alogliptin	Takeda				no forecast
DPP4	Jan-13	Jan-28	Nesina/Oseni	alogliptin	Takeda/other	84	480	564	Evaluate
SGLT2	Apr-13	Feb-29	Invokana	canagliflozin	JNJ	307	256	563	CS
SGLT2	Aug-14	Jul 27/Oct 29	Jardiance	empagliflozin	Lilly/BI	1772	1521	3293	Evaluate
SGLT2	Jan-14	Apr-26	Farxiga	dapagliflozin	AZN	732	2268	3000	CS
SGLT2	Jan-18	Jun-30	Steglatro	ertugliflozin	MRK/PFE	42	33	75	Evaluate
insulin -human	Oct-82	Apr-20	Humulin R	insulin lispro	Lilly	833	390	1223	Evaluate
insulin -human	Jn-86	Dec-02	Novolin (Human insulin)	inulin various	Novo	241	1198	1439	CS
insulin -basal	Jun-00	Feb-15	lantus (100 units/ml)	insulin glargine	Sanofi	1016	1927	2943	CS
insulin -basal	Aug-15	NA	Basaglar	insulin glargine	Lilly	588	305	893	Evaluate
insulin -basal	Aug-20	NA	Semglee	insulin glargine	Viatris	172	34	206	Evaluate
insulin -basal	2005	2018/2019	Levemir	insilin-determir	Novo	335	568	903	CS
insulin -basal	2015	to -2031	Toujeo	insulin glargine- longer acting	Sanofi	306	837	1143	CS
insulin -basal	2016	Jun-28	Tresiba	insulin glargine- longer acting	Novo	603	944	1547	CS
Insulin short acting	Jun-96	May-13	Humalog	insulin lispro	Lilly	1321	1132	2453	Evaluate
Insulin short acting	ept2001	Jun-17	Novolog/NovoRapid	insulin aspart	Novo	914	1620	2534	CS
Insulin short acting	Dec-04	Jun-18	Apidra	insulin glulisine	Sanofi	33	330	363	CS
Insulin short acting	Dec-17		Admelog	insulin lispro	Sanofi	25	115	140	CS
amylin analogue	Apr-05	Mar-19	Symlin	pramlintide	Amylin/AZN	<25	<25	<50	Evaluate
inhaled insulin	Feb-15	Jun-30	Afrezza	human insulin inhaled	Mannkind	40	0	40	Evaluate
GLP-daily - inj	Feb-12	Oct 25-31 (pen)	Bydureon	exenatide	AZN	321	64	385	CS
GLP-daily - inj	Jul-09	Feb-23	Victoza	liraglutide	Novo	1277	1116	2393	CS
GLP-daily - inj	Jan-17	Jul-25	Soliqua	lixisenatide	Sanofi	136	94	230	CS
GLP-daily - inj	Jul-14	Dec-22	Tanzeum	albiglutide	GSK/withdrawn				
GLP-weekly - inj	Feb-18	Dec-31	Ozempic	semaglutide	Novo	3683	1676	5359	CS
GLP-weekly - inj	Nov-14	Oct-28	Trulicity	dulaglutide	Lilly	4914	1558	6472	Evaluate
GLP - oral	Nov-19	Dec-31	Rybelsus	semaglutide - oral	Novo	675	94	769	CS
Other	Jun-98	Mar-10	Glucagen	glucagon	various				

Source: Company data, Credit Suisse , Evaluate Pharma estimates